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(54) Title: APPARATUS AND METHODS FOR MICROFLUIDIC APPLICATIONS

(57) Abstract: Non-rigid tape apparatus and fabrication methods for microfluidic processing applications such as gel electrophoresis are provided, where microfluidic processing is performed on selected areas. Parts of the tape are formed by high pressure plastic film forming. Membranes and other structures are self sealing during and after penetration by pipettes and electrical probes. Rigid exoskeleton elements protect the non-rigid parts during processing and facilitate transport of the tape.

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1 Apparatus and Methods for Microfluidic Applications

2

3 This invention relates to fabrication and processing
4 technology for microfluidic applications in chemical and
5 biological processing and analysis, in particular
6 fabrication and application of non-rigid apparatuses
7 optionally in the form of a tape.

8

9 In the field known as "lab-on-a-chip", electronic,
10 microfluidic and bio processes are combined at chip scale
11 to bring dramatic productivity and cost benefits to
12 fields as diverse as high throughput screening, bio-
13 molecular assays and point of care diagnostics.

14

15 Fabrication technologies are known that have been
16 developed in the microelectronics industry and then
17 applied to biotechnology and biomedical industries.

18 However, compared to electronic based devices,
19 biotechnology devices are much more diverse in order to
20 enable the manipulation of a large variety of bio
21 materials, fluids and chemicals. Improvements in
22 performance, throughput and cost have been achieved by
23 reducing the size and volume in miniaturised biosystems.

1

2 These "Lab-on-a-chip" solutions have increased the amount
3 of functionality per apparatus by miniaturisation. The
4 problem with increased miniaturisation is the complexity
5 of smaller scale processing and the large cost of
6 equipment for microfabrication. Furthermore,
7 conventional lithographic and etching processes adopted
8 from the microelectronics industry require rigid
9 apparatuses.

10

11 Glass apparatuses for microfluidic applications are
12 known, such as the LabCHIP from Caliper Technologies Corp
13 (Mountain View, CA), US Patent 6,274,089. The glass
14 apparatus is attached to a plastic moulded cartridge
15 which incorporates wells for loading test samples,
16 reagents and gel.

17

18 Rigid plastic apparatuses are known, such as the LabCard
19 from Aclara Biosciences Inc (Mountain View, CA), US
20 Patent 6,103,199. A tooling process involving patterning
21 and electroplating is used to create embossed
22 microchannels on the card surface.

23

24 "Lab-on-a-CD" devices such as from Gamera and Gyros use
25 centrifugal force of a rotating disk as the microfluidic
26 pumping mechanism, e.g., Gamera Bioscience Corporation
27 (Medford, MA), US Patent 6,063,589.

28

29 The above are all discrete devices which require further
30 handling steps for continuous operation. They are also
31 inefficient for single test operation.

32 Silicon apparatuses are known, such as the Nanogen chip,
33 which is a microfluidic microarray device, where the

1 microarray is selectively doped with biological or
2 chemical probes which can be polarised electrically to
3 attract or repel molecules from the sample material under
4 test.

5

6

7 For example, US Patent 5,858,195 to Lockheed Martin
8 Energy Research Corporation (Oak Ridge, TN) describes a
9 microchip laboratory system and method to provide fluid
10 manipulations. The microchip is fabricated using
11 standard photolithographic procedures and etching,
12 incorporating an apparatus and rigid cover plate joined
13 using die bonding. Capillary electrophoresis and
14 electrochromatography are performed in channels formed in
15 the apparatus. Analytes are loaded into a four-way
16 intersection of channels by electrokinetically pumping
17 the analyte through the intersection.

18

19 These approaches require time consuming additional steps
20 of picking and placing discrete apparatuses which
21 increases the overall processing cycle time in
22 microfluidic applications.

23

24 "MicroTape™ - A 384 Well Ultra High Throughput Screening
25 System" Journal of the Association for Laboratory
26 Automation, May 1999: Volume 4, Number 2, p. 31, Astle,
27 T.W., teaches of a tape device designed for storage of
28 liquid compounds in smaller volumes (typically 10 ul)
29 than the industry standard 96 or 384 well micro-titer
30 plate (MTP). Tape storage is in a pattern identical to a
31 384 well MTP. In effect, MicroTape™ is an alternative
32 passive storage medium to the micro-titer plate.

33

1 The primary features of MicroTape™ are:
2 1) bulk compounds typically stored in 96 or 384 well
3 micro-titer plates can be transferred into a smaller
4 volume storage medium, i.e. the MicroTape™, and then
5 stored within the medium for future use at low
6 temperature. When this array of compounds is required for
7 test, only one section of tape (i.e. a 384 well section)
8 need be retrieved and defrosted, rather than the whole of
9 the bulk compound medium.

10 2) the MicroTape™ incorporates a separate sealing
11 membrane to protect the compound during storage. This
12 membrane is capable of being de-sealed and re-sealed.
13 3) use of MicroTape™ for Polymerase Chain Reaction (PCR)
14 processing. The concept takes a reel/roll of MicroTape™
15 and uses alternate immersion in hot and cold water tanks
16 to perform thermal cycling for the PCR process.

17
18 The limitations of this approach are:
19

20 - It's well capacity is 10ul which is much larger scale
21 than lab-on-a-chip.
22 - It is not patterned microfluidic channels.
23 - It is not analytical, i.e. does not incorporate gels or
24 analytes through which molecular separation or
25 purification can be accomplished.
26 - It is not electrically active, i.e. incorporating
27 electrical elements or interfacing with electrical
28 elements i.e. it is simply a carrier.
29 - The PCR processing is performed on the whole reel
30 rather than on selectable areas or segments of the
31 tape.
32

- 1 In the contemporary art of gel electrophoresis, including
- 2 the emerging field of miniaturised systems, a common
- 3 means of detection is to capture an image of these layers
- 4 using electro-optical means. A convenient method is to
- 5 use a 2 dimensional CCD (Charged Coupled Device) detector
- 6 array (an area array) to capture the appearance of the
- 7 permeation layer area in a single "snapshot" image.
- 8 Another convenient method is to use a 1 dimensional CCD
- 9 array (a line array) and move it relative to the
- 10 permeation layer such that the full image is built up
- 11 from many adjacent line images.
- 12
- 13 It would be advantageous to provide an apparatus for
- 14 microfluidic applications that allowed an increased area
- 15 for microfluidic processing, without requiring an
- 16 increase in miniaturisation and the associated complexity
- 17 of processing.
- 18
- 19 It would be further advantageous to provide an apparatus
- 20 for microfluidic applications that facilitated loading
- 21 and transport of analytes and reagents both during and
- 22 after apparatus fabrication.
- 23
- 24 It would be further advantageous to provide an apparatus
- 25 that allowed continuous processing of a moving apparatus.
- 26
- 27 It would be further advantageous to provide an apparatus
- 28 that allowed a variable area on one apparatus, while
- 29 using a fixed size of apparatus handling mechanism.
- 30
- 31

1 It would further be advantageous to integrate information
2 storage and management systems within or on the apparatus
3 for use with simple detection methods.

4

5 It is an object of at least one aspect of the present
6 invention to provide an apparatus for microfluidic
7 applications.

8

9 It is a further object of at least one aspect of the
10 present invention to allow an increased area for
11 microfluidic processing and novel dynamic processing
12 steps both within and of the apparatus, while using
13 simple fabrication processes and apparatus handling
14 techniques.

15

16 In this document, a probe is defined as including
17 mechanical probes, electrical probes and pipettes for
18 fluidic manipulation.

19

20 In this document, indexing patterns are defined as
21 including patterns for facilitation mechanical movement,
22 detection of position, detection of movement, and display
23 and recording of information.

24

25 In this document, mass transport is defined as transport
26 of mass relative to the apparatus.

27

28 According to a first aspect of the present invention,
29 there is provided an apparatus for microfluidic
30 processing applications, wherein said microfluidic
31 processing is performed on a selected area of a plurality
32 of areas each individually selectable on said apparatus,
33 characterised in that the apparatus is non-rigid.

1
2 According to a second aspect of the present invention,
3 there is provided an apparatus for mass transport
4 microfluidic processing applications, characterised in
5 that the apparatus is non-rigid.

6

7 According to a third aspect of the present invention,
8 there is provided an apparatus for microfluidic
9 processing applications, characterised in that the
10 apparatus comprises at least one rigid member and at
11 least one non-rigid member.

12

13 Preferably the apparatus comprises at least two non-rigid
14 members.

15

16 Preferably said non-rigid member is a tape.

17

18 Preferably there are a plurality of rigid members each
19 associated with one of a plurality of areas each
20 individually selectable on said apparatus.

21

22 Preferably said rigid member comprises access ports.

23

24 According to a fourth aspect of the present invention,
25 there is provided a method of fabrication of an apparatus
26 for microfluidic processing applications, comprising the
27 step of attaching at least one rigid member to at least
28 one non-rigid member.

29

30 Preferably said method of fabrication further comprises
31 the step of forming at least one non-rigid member.

32

- 1 Preferably said step of forming said at least one non-rigid member comprises the step of high pressure plastic film forming with said high pressure acting on said apparatus.
- 5
- 6 Alternatively said step of high pressure plastic film forming is arranged with the high pressure acting on a compliant membrane, which is part of a forming tool in contact with said apparatus.
- 10
- 11 Preferably said rigid member has a maximum dimension perpendicular to its plane greater than the maximum dimension perpendicular to the plane of said at least one non-rigid member.
- 15
- 16 According to a fifth aspect of the present invention, there is provided a method of mounting an apparatus for microfluidic processing applications, comprising the step of attaching said apparatus to a non-rigid carrier that is in the form of a tape.
- 21
- 22 Preferably said carrier has a maximum dimension perpendicular to its plane greater than the maximum dimension perpendicular to the plane of said apparatus.
- 25
- 26 Preferably said apparatus is attached to said non-rigid carrier by snap fitting into apertures in said carrier.
- 28
- 29 Alternatively said apparatus is attached to said non-rigid carrier by ultrasonic welding, heat sealing, adhesive, chemical or molecular bonding.
- 32
- 33 Preferably said apparatus is a tape.

- 1.
- 2 Preferably said apparatus comprises a polymer film.
- 3.
- 4 Preferably said apparatus comprises processing elements
- 5 for microfluidic processing.
- 6.
- 7 Typically said processing elements comprise indents of
- 8 said apparatus.
- 9.
- 10 Optionally said processing elements comprise cavities
- 11 embedded within said apparatus.
- 12.
- 13 Optionally said processing elements comprise processing
- 14 materials in intimate contact with the surface of said
- 15 apparatus.
- 16.
- 17 Optionally said processing elements comprise processing
- 18 materials embedded within said apparatus.
- 19.
- 20 Optionally said processing elements comprise opaque,
- 21 translucent or coloured materials for providing optical
- 22 isolation between elements or providing indexing marks.
- 23.
- 24 Preferably an element of said apparatus is transparent.
- 25.
- 26 Preferably a member of said apparatus is transparent.
- 27.
- 28 Preferably said apparatus is penetrable.
- 29.
- 30 Preferably said apparatus is self sealing during
- 31 penetration.
- 32

10

1 More preferably said apparatus is self sealing after
2 penetration.

3

4 Preferably said apparatus further comprises an
5 impermeable membrane.

6

7 Preferably said impermeable membrane is affixed in
8 intimate contact with parts of the surface of said
9 apparatus.

10

11 Alternatively said impermeable membrane is arranged as
12 discrete areas of impermeable membrane in intimate
13 contact with parts of the surface of said apparatus.

14

15 Preferably said impermeable membrane is penetrable.

16

17 Preferably said impermeable membrane is self sealing
18 during penetration.

19

20 More preferably said impermeable membrane is self sealing
21 after penetration.

22

23 Optionally said impermeable membrane is re-sealed by a
24 capping element after penetration.

25

26 Preferably said impermeable membrane is supported by
27 support structures.

28

29 Preferably said apparatus further comprises a non-rigid
30 member.

31

32 Preferably said non-rigid member is affixed in intimate
33 contact with parts of the surface of said apparatus.

1
2 Alternatively said non-rigid member is arranged as
3 discrete areas of non-rigid member in intimate contact
4 with parts of the surface of said apparatus.

5
6 Preferably said non-rigid member is penetrable.

7.
8 Preferably said non-rigid member is self sealing during
9 penetration.

10
11 More preferably said non-rigid member is self sealing
12 after penetration.

13
14 Optionally said non-rigid member is re-sealed by a
15 capping element after penetration.

16
17 Preferably said non-rigid member is supported by support
18 structures.

19
20 According to a sixth aspect of the present invention,
21 there is provided a method of fabrication of an apparatus
22 for mass transport microfluidic processing applications
23 comprising the step of forming an apparatus that is non-
24 rigid.

25
26 According to a seventh aspect of the present invention,
27 there is provided a method of fabrication of an apparatus
28 for mass transport microfluidic processing applications
29 comprising the step of fabricating a tape.

30
31 Preferably said step of forming said apparatus comprises
32 the step of high pressure plastic film forming with said
33 high pressure acting on said apparatus.

- 1
- 2 Alternatively said step of high pressure plastic film
- 3 forming is arranged with the high pressure acting on a
- 4 compliant membrane, which is part of the forming tool in
- 5 contact with said apparatus.
- 6
- 7 Optionally said step of fabricating said apparatus
- 8 further comprises the step of preloading processing
- 9 materials onto said apparatus before fabrication.
- 10
- 11 Optionally said step of fabricating said apparatus
- 12 further comprises the step of loading processing
- 13 materials onto said apparatus during fabrication.
- 14
- 15 Typically said step of preloading or loading during
- 16 fabrication of said apparatus comprises the step of
- 17 depositing processing materials onto a carrier.
- 18
- 19 Typically said step of preloading or loading during
- 20 fabrication of said apparatus comprises the step of
- 21 depositing processing material onto a non-rigid member.
- 22
- 23 Preferably said deposited processing material comprises
- 24 permeation layers.
- 25
- 26 Alternatively said deposited processing material
- 27 comprises conductive material.
- 28
- 29 Alternatively said deposited processing material
- 30 comprises chemically or biologically active material.
- 31
- 32 Alternatively said deposited processing material
- 33 comprises marks for identity purposes.

- 1
- 2 Alternatively said deposited processing material
- 3 comprises magnetisable material.
- 4
- 5 Preferably said step of depositing comprises printing.
- 6
- 7 Alternatively said step of preloading or loading during
- 8 fabrication of said apparatus is performed by a
- 9 preloading or loading process selected from a list of
- 10 processes comprising: deposition and etching, injection
- 11 into a cavity and injection into an indentation.
- 12
- 13 Preferably said method of fabrication of said apparatus
- 14 further comprises the steps of depositing patterns on an
- 15 apparatus and forming said apparatus, wherein the
- 16 localised formation of said processing elements is
- 17 responsive to the distortion by said forming of said
- 18 deposited pattern.
- 19
- 20 Preferably said method of fabrication of said apparatus
- 21 further comprises the steps of depositing patterns on an
- 22 apparatus and localised formation of said apparatus is
- 23 responsive to the topography of said deposited pattern,
- 24 resulting in the formation of said processing elements.
- 25
- 26 Preferably said step of depositing comprises pre-
- 27 printing.
- 28
- 29 According to an eighth aspect of the present invention,
- 30 there is provided a method of fabrication of an apparatus
- 31 for mass transport microfluidic processing applications,
- 32 comprising the step of including an impermeable membrane
- 33 as part of said apparatus.

1
2 Preferably said step of including an impermeable membrane
3 comprises the step of affixing an impermeable membrane to
4 a substrate.

5
6 Optionally, said step of including an impermeable
7 membrane comprises the step of depositing, overlaying or
8 affixing discrete areas of impermeable membrane in
9 intimate contact with parts of the surface of said
10 apparatus.

11
12 Optionally, said step of including an impermeable
13 membrane comprises the step of depositing, overlaying or
14 affixing an impermeable membrane on said apparatus and
15 selectively removing areas of said impermeable membrane.

16
17 Optionally, said selected removal of said impermeable
18 membrane is performed by the step of cropping.

19
20 According to a ninth aspect of the present invention,
21 there is provided a method of fabrication of an apparatus
22 for mass transport microfluidic processing applications,
23 comprising the step of including a non-rigid member as
24 part of said apparatus.

25
26 Preferably said step of including a non-rigid member
27 comprises the step of affixing a non-rigid member to a
28 substrate.

29
30 Optionally, said step of including a non-rigid member
31 comprises the step of depositing, overlaying or affixing
32 discrete areas of non-rigid member in intimate contact
33 with parts of the surface of said apparatus.

1
2 Optionally, said step of including a non-rigid member
3 comprises the step of depositing, overlaying or affixing
4 a non-rigid member on said apparatus and selectively
5 removing areas of said non-rigid member.

6

7 Optionally, said selected removal of said non-rigid
8 member is performed by the step of cropping.

9

10 According to a tenth aspect of the present invention,
11 there is provided a method of microfluidic processing,
12 comprising the steps of selecting an area of a plurality
13 of areas of an apparatus and performing microfluidic
14 processing at said selected area, characterised in that
15 said apparatus is non-rigid.

16

17 Optionally said step of performing microfluidic
18 processing comprises contacting at least one conducting
19 element that connects the exterior of said apparatus to
20 the interior of said apparatus.

21

22 Preferably said method further comprises the step of
23 providing an electrical potential to at least one
24 conducting element.

25

26 Preferably said method further comprises the step of
27 enabling an electrical current to pass through said least
28 one conducting element.

29

30 Preferably said apparatus is a tape.

31

32 Preferably said microfluidic processing is mass transport
33 microfluidic processing.

1

2 Preferably said microfluidic processing is responsive to
3 the deformation of said apparatus.

4

5 Preferably said deformation comprises deformation by a
6 step selected from a list of steps comprising: bending,
7 flexing, folding, twisting, conforming to a rigid
8 surface, mechanical deformation, deformation by applying
9 a sound pressure, deformation by applying a liquid
10 pressure, and deformation by applying a gas pressure.

11

12 Typically said gas pressure is a negative pressure.

13

14 Optionally said deformation may further comprise the step
15 of bringing part of said apparatus back into contact with
16 another part of itself.

17

18 Alternatively, said step of deformation further comprises
19 the step of bringing a part of said apparatus into
20 contact with another apparatus.

21

22 Optionally said deformation of said apparatus comprises
23 the step of moving part of said apparatus into a position
24 for processing of said part of said apparatus.

25

26 Typically said position for processing is a position with
27 said apparatus in contact with a processing tool.

28

29 Preferably said microfluidic processing is responsive to
30 said deformation of said apparatus, said microfluidic
31 processing being selected from a list comprising pumping,
32 filling, pouring, pressurising, mixing, dispensing,
33 aspirating, separating, combining, heating and cooling.

1

2 According to an eleventh aspect of the present invention,
3 there is provided a method of processing for microfluidic
4 processing applications, characterised in that the
5 processing comprises the step of piercing an impermeable
6 membrane.

7

8 Preferably said step of piercing an impermeable membrane
9 is performed with at least one probe.

10

11 Optionally said at least one probe comprises at least one
12 pipette.

13

14 More preferably said method of processing further
15 comprises the step of providing an electrical potential
16 to at least one conducting probe that has pierced said
17 membrane.

18

19 Alternatively said step of processing further comprises
20 the step of enabling an electrical current to pass
21 through at least one conducting probe that has pierced
22 said membrane.

23

24 According to a twelfth aspect of the present invention,
25 there is provided a method of processing for microfluidic
26 processing applications, characterised in that the
27 processing comprises the step of piercing an apparatus.

28

29 Preferably said apparatus is self sealing during said
30 step of piercing.

31

32 Preferably said apparatus is self sealing after said step
33 of piercing.

1
2 Optionally said apparatus is re-sealed by a capping
3 element after penetration.

4
5 Preferably said step of piercing the apparatus is
6 performed with at least one probe.

7
8 Optionally said at least one probe comprises at least one
9 pipette.

10
11 More preferably said method of processing further
12 comprises the step of providing an electrical potential
13 to at least one conducting probe that has pierced said
14 apparatus.

15
16 Alternatively said step of processing further comprises
17 the step of enabling an electrical current to pass
18 through a conducting probe that has pierced said
19 apparatus.

20
21 According to a thirteenth aspect of the present
22 invention, there is provided an apparatus for
23 microfluidic processing applications, characterised in
24 that the apparatus is a non-rigid tape comprising a
25 plurality of indexing patterns.

26
27 Preferably said indexing patterns are rigid members.

28
29 Preferably said indexing patterns are repeated.

30
31 Preferably said indexing patterns are arranged to
32 facilitate detection of position.

33

1 Typically said indexing patterns are arranged to
2 facilitate detection of position using optical detection.

3

4 According to a fourteenth aspect of the present
5 invention, there is provided a method of transporting a
6 tape apparatus for microfluidic applications comprising
7 the step of moving said apparatus by interaction of a
8 moving object with at least one rigid member attached to
9 said apparatus.

10

11 In order to provide a better understanding of the present
12 invention, an embodiment will now be described by way of
13 example only and with reference to the accompanying
14 figures in which:

15

16 Figure 1 illustrates in schematic form non-rigid
17 apparatuses, showing a section of tape and an enlargement
18 of one area suitable for gel electrophoresis in
19 accordance with the present invention;

20

21 Figure 2 illustrates in schematic form a variety of
22 processing elements in accordance with the invention;

23

24 Figure 3 illustrates processing elements incorporating
25 impermeable membranes comprising homogeneous apparatus
26 material;

27

28 Figure 4 illustrates impermeable processing elements
29 incorporating discrete impermeable membranes and
30 processing elements on hinged tabs;

31

- 1 Figure 5 illustrates the insertion and removal of a probe
- 2 into a processing element through an impermeable self-
- 3 sealing membrane;
- 4
- 5 Figure 6 illustrates a plan view of an apparatus
- 6 incorporating an extended impermeable membrane with a
- 7 variety of support structures;
- 8
- 9 Figure 7 illustrates a cross-section of the same
- 10 structures illustrated in Figure 6;
- 11
- 12 Figure 8 illustrates some of the same structures in
- 13 cross-section as Figure 7, but where the processing
- 14 elements comprise processing materials;
- 15
- 16 Figure 9 illustrates in schematic form a plan view of a
- 17 structure for probing through an impermeable membrane;
- 18
- 19 Figure 10 illustrates an alternative arrangement to that
- 20 of Figure 9 where the channel extends into the apparatus;
- 21
- 22 Figure 11 illustrates a cross-section of the structure
- 23 illustrated in Figure 10;
- 24
- 25 Figure 12 illustrates a tape apparatus with indexing
- 26 patterns;
- 27
- 28 Figure 13 illustrates in schematic form a variety of
- 29 cross-sections of indexing patterns;
- 30
- 31 Figure 14 illustrates a flow chart describing the steps
- 32 of fabrication of an apparatus;
- 33

1 Figures 15 and 16 illustrate arrangements of scanning the
2 optical detectors for scanning the apparatus;

3

4 Figure 17 illustrates plan and elevation views of a
5 micro-array configuration of the apparatus;

6

7 Figure 18 illustrates in schematic form non-rigid
8 apparatuses in accordance with the present invention;

9

10 Figure 19 illustrates in schematic form the components of
11 a planned fabrication scheme of one embodiment;

12

13 Figure 20 illustrates in schematic form a compact
14 fabrication option;

15

16 Figure 21 illustrates in schematic form an operating mode
17 using a vacuum suction onto a scanner or a
18 heating/cooling plate;

19

20 Figure 22 illustrates in schematic form reservoir
21 fabrication showing the option of sample loading through
22 penetration of a cover seal;

23

24 Figure 23 illustrates in schematic form reservoir
25 fabrication showing the option of electrical probe
26 penetration of a cover seal;

27

28 Figure 24 illustrates in schematic form an alternative
29 electrical probe option;

30

31 Figure 25 illustrates in schematic form a supporting
32 layer of one segment of a tape after preparatory
33 printing;

- 1
- 2 Figure 26 illustrates in schematic form a formed pattern
- 3 layer after forming;
- 4
- 5 Figure 27 illustrates in schematic form a formed pattern
- 6 layer after a blanking operation;
- 7
- 8 Figure 28 illustrates in schematic form a formed pattern
- 9 layer assembled to the supporting layer;
- 10
- 11 Figure 29 illustrates in schematic form an exoskeleton;
- 12
- 13 Figure 30 illustrates in schematic form an exoskeleton
- 14 affixed to the supporting/patterned layer;
- 15
- 16 Figure 31 illustrates in schematic form a section
- 17 (vertical scale exaggerated for clarity) and plan view
- 18 through one tape segment and disposition of sealing
- 19 plugs;
- 20
- 21 Figure 32 illustrates in schematic form loading of
- 22 electrolyte during manufacture;
- 23
- 24 Figure 33 illustrates in schematic form loading of
- 25 analyte during manufacture; and
- 26
- 27 Figure 34 illustrates in schematic form loading of a test
- 28 sample at the point of use.
- 29
- 30 Figure 35 illustrates in a flowchart of automated
- 31 processing using the fabricated tape.
- 32

1 The invention is a non-rigid apparatus for microfluidic
2 processing applications, which may be in the form of a
3 tape. The use of a non-rigid apparatus allows novel
4 dynamic processing methods. The incorporation of re-
5 sealable impermeable layers allows further novel dynamic
6 processing steps.

7

8 Figure 1a shows a typical section of tape 1 with an array
9 of microfluidic processing areas or processing segments 2
10 in accordance with a preferred embodiment of the present
11 invention. Adjacent test segments are spaced to suit the
12 sample supply vessel. For example, where samples are
13 delivered for test in a 384 well microtiter plate format,
14 the tape segments will be supplied on a 4.5mm pitch, P.
15 The tape is processed in a vertical plane with the sample
16 loading ports uppermost. The tape width, W, is typically
17 25mm but is configurable in a range of 1mm to 100mm.

18

19 Figure 1b shows an enlargement of a single processing
20 segment 2, the operation of which follows well-
21 established principles of electrophoresis. A DNA test
22 sample is assumed.

23

24 The apparatus includes a supporting layer 251, a formed
25 pattern layer 265 with a machine readable index mark 254.
26 The pattern layer has formed cavities 266 and a
27 connecting channel 267 filled with gel. The exoskeleton
28 2915 supports plugs 3124 that are used for re-sealable
29 access to the cavities.

30

31 A DC voltage in the range 5 to 500 Volts (typically
32 100V/cm has been found to be suitable) will be applied
33 across negative terminal 252 and positive terminal 253.

1 This will cause the negatively charged DNA sample 3430 to
2 migrate into the gel column 267 and its constituent
3 molecules will then separate into bands in accordance
4 with their molecular weight. An image of the band pattern
5 will be captured by a commercial CCD camera and the image
6 processed and presented to the user on a computer screen.

7

8 The electrical terminal pads 252 and 253 are conveniently
9 presented for perpendicular access by external contact
10 pins whose engagement will be controlled by the tape
11 processing instrument. The exoskeleton 2915 may be
12 conveniently employed as the tape transport means, and be
13 driven by, for example, a toothed belt or a drive pinion
14 having the same tooth pitch as the test segments on the
15 tape.

16

17 The CCD image capture system can also conveniently
18 capture the test segment ID mark, thus avoiding the need
19 for a separate device such as a bar code reader.

20

21 Figure 2a illustrates a part of an apparatus 20 in cross-
22 section. The apparatus contains a variety of processing
23 elements which are an indent 21, a void or cavity in the
24 apparatus 22 processing materials on the surface of the
25 apparatus 23, processing materials embedded within the
26 apparatus 24, and processing materials in an indent on
27 the surface of the apparatus 25.

28

29 Figure 2b illustrates part of an apparatus in cross-
30 section with processing materials partially filling the
31 height of a cavity in the apparatus 26 and processing
32 material 27 embedded in a channel 28 within the
33 apparatus.

1
2 The processing elements may comprise geometries which
3 have sloping, curved or stepped surfaces. The processing
4 materials may be conformal layers in intimate contact
5 with surfaces of the apparatus. The processing elements
6 may be opaque, translucent or coloured in order to
7 provide optical isolation between elements or,
8 alternatively, to provide indexing marks for allowing
9 detection of movement and position of the apparatus.

10
11 Several of the processing elements shown in Figures 2a
12 and 2b may be linked together, for example by cavities
13 or indented troughs, which are themselves processing
14 elements such that the linked elements act as a single
15 processing group.

16
17 Figure 2c illustrates a plan view 210 of processing
18 element groups 211 on part of an apparatus 212. Figure
19 2d illustrates a cross section of one of the processing
20 element groups 211 shown in figure 2c. The formed
21 plastic substrate 212 has a plastic membrane film 213
22 attached 214. The membrane is typically 0.1mm thick, but
23 could be as thin as 0.02mm. An indented trough 215 is
24 provided for processing materials such as materials based
25 on Agarose or polyacrylamide gel. A channel 216 is
26 provided for a plug that can be removed by, for example,
27 laser ablation in order to allow processing material
28 transport between the indented trough 215 and another
29 processing element, indent 217. The substrate indents
30 have pips 218 that are shaped to guide a probe such as a
31 pipette to an area of the lower surface for penetration
32 into the processing elements, for example indent 217.

1 The substrate may be self-sealing during and after such
2 penetration.

3

4 The processing materials can be gases, liquids, solids or
5 semi-solids, e.g. biomolecular samples, fragments of
6 DNA, biochemical polymers, chemical polymers,
7 biomolecular modifiers, catalysts, antibodies,
8 polypeptide molecules, protein molecules, biological
9 organisms such as cells and viruses and permeation
10 layers. The permeation layers may be solid, semi-solid,
11 liquid, viscous, gelatinous or gaseous layers. The
12 permeation layers may be biomolecular gates which are
13 activated by electrical probes. The function of the
14 biomolecular gates is defined by their particular depth,
15 shape, volume and composition.

16

17 Figure 3 shows a cross-section 30 of an apparatus for
18 microfluidic processing applications. The apparatus
19 contains a processing element 31 that is a cavity in the
20 apparatus material. At the top of the cavity the
21 apparatus material is thin, such that there is a membrane
22 32 that is impermeable and acts as an hermetic seal to
23 protect the contents of the cavity.

24

25 The apparatus contains another processing element 33,
26 where the membrane is configured as a flap 34, such that
27 the cavity is sealed when the unattached end of the
28 membrane is in contact with the apparatus 35.

29

30 Figure 3 illustrates another processing element 36 with a
31 membrane arranged as a flap 37 and distortion of the
32 apparatus 38 resulting in the opening of the flap at its
33 unattached end 39.

1
2 Figure 4a illustrates an apparatus 40 that includes the
3 same type of processing elements as shown in Figure 3,
4 but in this case the impermeable membrane is deposited,
5 overlaid or affixed as discrete areas of impermeable
6 membrane in intimate contact with parts of the surface of
7 the apparatus. In the first processing element 41, the
8 impermeable membrane 42 provides a hermetic seal to the
9 cavity 43.

10
11 Another processing element 44 shows the impermeable
12 membrane 45 in intimate contact and attached to the
13 apparatus at the left hand side 46 and configured as a
14 flap in a sealing contact with the right hand side 47 of
15 an indent in the apparatus 48. This flap may be opened
16 by deforming the apparatus in the same way as described
17 as above with reference to processing element 36.

18
19 In another processing element 49, the impermeable
20 membrane 410 is deposited as a plug in an indent
21 resulting in a cavity 411, the membrane again providing
22 an hermetic seal.

23
24 Alternatively, the impermeable membrane is continuous
25 with the tape (i.e. not discrete). This continuous
26 configuration can also embody local flaps in the membrane
27 and still be one continuous membrane.

28
29 Figure 4b illustrates a plan view and Figure 4c
30 illustrates cross-section views of a strip of apparatus
31 413 where a section of the apparatus had been removed 412
32 by punching out. The shape punched out has left several
33 tabs 414 each with an indent 415 for containing

1 processing materials. The tab 414 may be mechanically
2 folded along the fold line 417. The fold line may be
3 weakened by perforation or indenting. A second indent
4 for processing materials 418 is positioned on the
5 opposite side of the fold line from the indent 415. When
6 the tab is folded over 419, the indent 415 is tipped over
7 into contact with the indent 418, allowing mixing,
8 pouring or transfer of processing materials between the
9 two indents. This pouring may be assisted by the force of
10 gravity, capillary action or external pressure.
11 Alternative arrangements can be made that tilt through an
12 angle of e.g. 30 degrees to cause pouring.

13
14 Figure 5 shows a cavity during a sequence of steps before
15 penetration 51, during penetration 52 and after
16 penetration 53. The probe 54, which is a pipette, is to
17 be inserted into the cavity 55 through the membrane 56.
18 When the probe 57 is inserted through the membrane 58,
19 the membrane is self-sealing, such that there is a seal
20 between the probe and the membrane 58. Processing
21 materials 510 are then deposited in the cavity. After
22 removal of the probe 511, the impermeable membrane is
23 self-sealing and a seal 512 is formed at the exit point
24 of the probe. The penetration of the impermeable
25 membrane can allow introduction of processing materials
26 into cavities in the apparatus or removal of processing
27 materials from the apparatus, the penetration of the
28 membrane can allow the introduction of measurement tools
29 into the apparatus or processing tools into the
30 apparatus. When penetration is by a conducting probe,
31 voltages can be applied that cause movement of fluids
32 through processing materials using an electrokinetic
33 method.

1
2 Large areas of membrane would tend to bend on attempted
3 insertion of a probe. Figure 6 shows a plan view of an
4 apparatus 60 with an extended membrane 61 and support
5 structures that provide support for the membrane adjacent
6 to the location where probes are to penetrate the
7 membrane. Figure 7a shows a cross-section 70 of the same
8 structure that is shown in the plan view of Figure 6.
9 Figure 7b shows a cross-section 71 of the same structure
10 that is shown in the plan view of Figure 6, but with a
11 continuous membrane 72 affixed to a substrate.

12
13 Figures 6 and 7 include support structures that are
14 pillars 62, ribs 63 and an annulus 64. The centre of the
15 annulus contains a membrane that may be penetrated by a
16 probe. The annulus allows a "via" hole 65 to be created
17 all the way through the apparatus and through which a
18 wire or conducting probe can be passed so that a magnetic
19 field can be created to interact with the adjacent
20 processing area of the apparatus.

21
22 Another useful structure is a circular indent but still
23 connected to adjacent processing elements and an
24 externally configured loop or coil of wire (or other
25 conducting element) around that circular indent. The
26 electrical/magnetic field created can be used to attract
27 or trap or process the liquid in the circular indent.

28
29 A "U" shaped pillar 66 is shown and a probe that enters
30 in the centre of the "U" at point 67, marked with a plus,
31 may be connected to a probe penetrating the impermeable
32 membrane at the second penetration point 68 by an
33 electrical, liquid or permeation path that is greater in

1 length than the direct distance between the two
2 penetration points.

3

4 Figure 8 shows a cross-section 80 of similar structures
5 to those in Figure 7, except that the cavities in the
6 apparatus are filled with processing materials 81.

7

8 Figure 9 shows a plan view of an apparatus 90 with a
9 membrane that extends from a first penetration point 91
10 to a second penetration point 92 via an indented trough
11 93. A probe inserted through the impermeable membrane at
12 the first penetration point 91 may be connected to a
13 probe penetrating the impermeable membrane at the second
14 penetration point 92 by an electrical, liquid or
15 permeation path that is greater in length than the direct
16 distance between the two penetration points.

17

18 Figure 10 shows a plan view of an apparatus 100 with two
19 membranes, each of which are penetration points 101 and
20 102. The dotted lines represent the edges of a buried
21 channel 103 in between the two membranes.

22

23 Figure 11 shows a cross-section through the line
24 connecting the two penetration points of Figure 10 which
25 can be seen to be two membranes 101 and 102. The channel
26 103 extends into the depth of the apparatus 104. In this
27 alternative arrangement the electrical, liquid or
28 permeation path between tips of probes that are inserted
29 through the penetration points are also greater than the
30 direct distance between the two probes.

31

32 Turning Figures 10 and 11 through 90 degrees, illustrates
33 side entry (rather than top entry) to the apparatus.

1 Then Figure 10 becomes a side view of the tape and Figure
2 11 is a plan view of the plane of a strip of tape.
3
4 With reference to Figure 12, an apparatus 120 is shown in
5 plan view with a plurality of indexing patterns 121. The
6 indexing patterns may be opaque, translucent or coloured
7 materials. The indexing patterns may be surface
8 patterns, such as indents or recesses or raised
9 patterns of apparatus material, for example the
10 exoskeleton (2915 in Figures 1b and 29). Alternatively,
11 the indexing patterns may be embedded within the
12 apparatus or patterns of magnetism in a magnetic film or
13 perforations through the depth of the apparatus. Indexing
14 patterns are arranged to facilitate traction of the
15 apparatus and detection of position using optical,
16 electromagnetic, electrochemical, electrical or other
17 forms of detection. The indexing patterns may also
18 record information related to the apparatus processing
19 elements or the apparatus processing materials on the
20 apparatus or within it processing results, processing
21 status, processing time, processing location or
22 processing identity. An indexing pattern may be a strip
23 of material which functions as a data recording medium,
24 for example magnetic or magneto-optical tape. Such tape
25 may be written to and read by standard methods.
26
27 With reference to Figure 13 that shows in schematic form
28 a variety of cross-sections of indexing patterns, an
29 indexing pattern is shown as an indent 130, a raised
30 feature 131, an embedded feature 132 or a hole 133
31 punched through the apparatus.
32

1 With reference to Figure 14a, a flow chart is shown which
2 describes the general process steps for the fabrication
3 of non-rigid apparatuses for microfluidic processing
4 applications, including apparatuses in the form of a tape
5 or apparatuses of homogeneous material which may be
6 assembled to a tape or discrete microfluidic devices
7 which may be assembled to a tape.

8

9 Firstly, raw material preparation is provided, 141, the
10 primary material will be a flexible substrate, preferably
11 in the form of a continuous tape but other substrates,
12 membranes, films, mouldings, skeletal structures or pre-
13 assembled microfluidic devices may be part of the
14 fabrication "kit".

15

16 Patterns can be pre-printed 142, preferably on a flat
17 plastic non-rigid substrate. These patterns may be
18 conductive elements, chemically or biologically active
19 zones, magnetisable zones, or printed marks for identity
20 purposes.

21

22 The apparatus, 143, is formed using high pressure thermo-
23 forming with the high pressure acting on the apparatus or
24 the high pressure acting on a compliant membrane which is
25 part of the forming-tool that is in contact with the
26 apparatus. The high pressure may be delivered by a gas
27 or a fluid. During forming, the pre-printed patterns on
28 the tape surface may be distorted in response to the
29 topography of the formed processing elements. The final
30 position of the pre-printed pattern material may be
31 predicted by calibration test runs or simulation in order
32 to design pre-printed patterns that distort to create
33 processing elements that comprise the processing material

1 that has been pre-printed. Alternatively, the forming of
2 an apparatus may be performed by stereolithography or
3 selective laser sintering. While forming the apparatus
4 by stereolithography or selective laser sintering,
5 processing elements may be included in the apparatus
6 either by direct patterning or in response to the
7 topography of the pre-printed patterns on the carrier.
8

9 The fabrication of the apparatus can further comprise the
10 step of preloading processing materials 144. These
11 processing materials may be preloaded by processes such
12 as printing, film deposition and etching, stereo-
13 lithography, injecting into a cavity and also injection
14 into an indentation. Alternatively, the preloading may
15 be achieved by tilting the apparatus with respect to
16 gravity in order to open flaps of impermeable membrane so
17 as to introduce processing materials through the open
18 flaps into underlying structures. Alternatively these
19 flaps may be opened by the distortion of the apparatus,
20 such as conforming it to a rigid roller or corner.
21

22 A cropping operation 145 can be incorporated (optionally
23 before the preloading step) to insert apertures in a
24 substrate or finish a substrate to a defined external
25 profile.
26

27 Apparatus assembly can continue, 146, by attachment or
28 assembly of other layers, for example, a sealing layer or
29 sealing layers, or sealing plugs, or additional
30 supporting layers to improve the robustness of the
31 apparatus, or other pre-assembled devices. The attachment
32 methods may include a mechanical snap-fit, a mechanical
33 interference fit, ultrasonic welding, heat sealing,

1 molecular, chemical or adhesive bonding. Typically the
2 final layer of apparatus that is affixed results in one
3 or more impermeable membranes as part of the apparatus.
4 Alternatively, the membranes may be formed by depositing,
5 overlaying or affixing discrete areas of impermeable
6 membrane in intimate contact with parts of the surface of
7 the apparatus. Alternatively the formation of the
8 impermeable membrane may be performed by depositing a
9 film of impermeable membrane across the apparatus and
10 selectively removing areas of the impermeable membrane.
11 This selective removal may be performed using
12 cropping/blanking or by lithography, such as
13 photolithography, for patterning combined with wet or dry
14 etching. These membranes are optionally formed of
15 homogeneous apparatus material in the case of formation
16 using stereo-lithography or selective laser sintering.
17
18 The apparatus can incorporate a further loading sequence,
19 147, of chemical or biological agents such as solvents,
20 electrolytes, gels, stainers, dyes, affinity tags or bio-
21 sensors. This loading may be achieved by pipette probe
22 through the apparatus membrane or through an access port
23 or access ports in the apparatus.
24
25 These steps 141 to 147 have many possible permutations
26 and Figures 14b, 14c and 14d illustrate by way of
27 example, the fabrication sequence of some of the
28 alternative embodiments described within this document.
29
30 Figure 14b shows the general fabrication sequence for the
31 three layer construction method described by Figure 19
32 including the fabrication steps 14191, 14192 and 14193 of

1 the substrate 191 sealing layer 192 and carrier layer 193
2 respectively.

3

4 Figure 14c shows the general fabrication sequence for the
5 three layer construction method described by Figure 22,
6 including the fabrication steps 14221, 14222 and 14225 of
7 the substrate 221 sealing layer 222 and carrier layer 225
8 respectively.

9

10 Figure 14d shows the general fabrication sequence for the
11 construction method described by Figure 1b including the
12 fabrication steps 14251, 14265, 142915 and 143124 of the
13 substrate 251 process layer 265, exoskeleton 2915 and
14 sealing caps 3124 respectively.

15

16 In each of Figures 14a to 14d, the material preparation
17 step 141 is a film forming step, except for the
18 exoskeleton and sealing cap material preparation 1411,
19 which is a moulding step.

20

21 With reference to Figure 15, the moving apparatus 150
22 with indexing patterns that are permeation (for
23 separation) indents 151, can provide the scanning
24 function of a scanning optical detector with fixed optics
25 152 and a fixed line scan Charged Coupled Device (CCD)
26 detector 153.

27

28 Additionally, with reference to Figure 16, when this
29 fixed scanning system 161 is configured to suit a chosen
30 width of tape apparatus 162 (e.g. 100mm, shown in plan
31 view, not to scale) or multiple transverse separation
32 layers, then it can also image capture, without
33 modification, any other tape apparatus which is of lesser

1 width 163 (e.g. 50mm or 20mm), thus providing the
2 advantage of a detection system with flexibility in the
3 handling of different widths of substrate.

4

5 Additionally, where the substrate is configured to have
6 more than one discrete permeation layer in a transverse
7 line across the substrate, each of these more than one
8 discrete permeation layers can be imaged simultaneously.

9

10 In the emerging field of biological micro-arrays, the
11 processing substrates are typically comprised of a rigid
12 transparent material (e.g. a glass slide) and whereby
13 bio-material is deposited locally on a rectangular grid
14 whose pitch may be in the range of 50um to 2mm. The
15 present invention provides the advantage that it is
16 equally suitable as a substrate for micro-array
17 fabrication but offers the benefit of having low
18 fabrication cost and a capability for continuous
19 processing due to the flexible nature of the apparatus in
20 its form as a continuous tape.

21

22 With reference to Figure 17, the apparatus is illustrated
23 schematically 170 in plan and side views configured to
24 locate each element of a micro-array 171 in a shallow
25 well or dimple 172, on a tape 173, thereby allowing a
26 reduced risk of cross contamination between adjacent
27 elements.

28

29 The apparatus is thus configured to provide an improved
30 degree of containment for any reaction process which is
31 specified to take place on that micro-array element and
32 that this improved degree of containment can allow

1 operations of mixing, stirring or agitation which would
2 not be achievable with planar micro-arrays.

3

4 The apparatus is configured such that this shallow well
5 has a thin wall section 174 (e.g. 0.1mm, compared to a
6 glass slide of typically 1 to 3mm) that enables the
7 efficient coupling of a conductive heating element 175
8 (for example a peltier device or similar) to the well for
9 the purpose of, for example, hybridisation of a DNA
10 sample at a temperature in the range of, for example, 60
11 to 80 degrees centigrade.

12

13 This thin wall section can readily be transparent and
14 that this enables the efficient coupling of an optical
15 system 175 to detect the bio-reaction state of any
16 element on the micro-array.

17

18 The apparatus can also have different regions
19 functionalised for the attachment of chemical or
20 biological moieties such as affinity tags or biological
21 probes. Within a microfluidic channel, there can be
22 micro-zones incorporating reactive groups for highly
23 specific functions, e.g. an affinity tag such as a
24 streptavidin coated zone.

25

26 With reference to Figure 18, an apparatus 10 according to
27 the present invention is shown. The apparatus 11 is non-
28 rigid and is shown as being bent, by the apparatus being
29 conformed to the surface of a roller 12.

30

31 The apparatus is non-rigid in that it is pliant, unlike
32 rigid apparatuses known in the prior art that are made of
33 at least one layer of hard plastic or glass or silicon,

1 or where the composite apparatus is rigid. On
2 deformation of the apparatus according to the present
3 invention, the apparatus can return to its original shape
4 (i.e. flat) after deformation. The apparatus may have a
5 bend radius approaching zero.

6

7 The apparatus is a tape in that it is substantially
8 longer than it is wide in its larger two dimensions.
9 Hence it is a substantially continuous, narrow, flexible
10 strip. The tape 13 may be arranged in a reel-to-reel
11 arrangement between reels or rollers 14 and 15.

12

13 With extreme deformation, the apparatus may be folded and
14 remain folded. This may be facilitated by using
15 perforations or indentations to weaken the fold line.
16 Thus the apparatus may be folded into a fanfold
17 arrangement 16 for storage, dispensing and processing.

18

19 The tape can also be separated into short discrete
20 sections 17. The separation may be performed by
21 guillotining or tearing across perforations or
22 indentations in the tape.

23

24 A continuous strip of tape 18 may be arranged around
25 rollers 19 into a conveyor belt arrangement. A twist in
26 the tape would provide a Moebius strip arrangement.

27

28 The apparatus may be formed from a polymer film, that is
29 a thermoplastic polymer film, thermosettable polymer
30 film, elastomeric polymer film or hybrid compositions of
31 each of these films.

32

1 In another embodiment, the tape comprises three primary
2 construction elements as illustrated with reference to
3 Figure 19. The tape incorporates a thin polymer substrate
4 191 that is formed to create indented wells, channels and
5 junctions which can be configured to create a wide range
6 of micro-fluidic geometries. This substrate may
7 optionally incorporate one or more surface coating layers
8 on the processing side of the substrate and these
9 layer(s) may fully cover the substrate surface or be
10 confined to local areas of the substrate. The substrate
11 may incorporate liquid or solid chemicals within the well
12 or channel areas of the substrate.

13

14 The substrate and its chemical contents may be protected
15 by the attachment of a cover seal 192 membrane. The
16 combined substrate and cover seal will be attached to a
17 carrier layer 193 whose function is to protect the
18 substrate from mechanical stress or damage during
19 handling, shipment, storage or end user processing. The
20 tape may be a one time use consumable item.

21

22 The tape assembly employs construction materials,
23 fabrication techniques and packaging methods that ensure
24 that the tape will function reliably at its final point
25 of use. The tape will therefore be unaffected by:

- 26 - Automated and manual handling processes prior to
27 shipment packaging (factory);
- 28 - Automated and manual handling processes at the point of
29 use (end user);
- 30 - Shipment transport (protected by secondary packaging);
- 31 - Transport temperatures of -40C to +70C (up to 24
32 hours);
- 33 - Storage temperatures of 0C to +40C (up to 12 months);

- 1 - Relative humidity in range 10% to 90% (transport and storage); and
- 2 - Atmospheric pressure (air cargo).

4

5 The substrate comprises a thin polymer membrane with a
6 thickness of 50um preferred, but 125um for some
7 applications. The thickness may be selected to match
8 available commercial film grades.

9

10 The substrate has:

- 11 - Forming radius equal to thickness without stress
12 cracking;
- 13 - Feature width to depth ratio, typically in range 2:1 to
14 1:1;
- 15 - Uniform (consistent) draw during forming.

16

17 Thermal assist during (or prior to) forming is desirable.

18 Forming may be:

- 19 1) high pressure in range 1 bar to 200 bar
- 20 2) Vacuum
- 21 3) high pressure with vacuum assistance

22

23

24 All of these may benefit from a pre-heating cycle.

25

26 Desirable features of the substrate include:

- 27 - stable after forming (having no shape memory effects);
- 28 - Flexible, non rigid, non brittle;
- 29 - Abrasion Resistant;
- 30 - Punchable, to create optional holes for mechanical
31 indexing;
- 32 - Penetratable by probe (e.g. for liquid delivery or for
33 electrical probing);

- 1 - High optical clarity;
- 2 - Adaptable via suitable surface modification to minimise static charge or to locally influence hydrophilic/hydrophobic surface characteristics;
- 3 - Chemical Resistance to Aqueous solutions
- 4 - Analyte material loaded in the substrate channels typically comprised of Agarose or Polyacrylamide,;
- 5 - Provide bio-compatible surface (e.g. DNA, proteins, cells, bacteria etc);
- 6 - Avoid leaching of metals, anti-oxidants and stabilisers;
- 7 - Capable of receiving a heat sealable cover layer e.g. polyester/polyethylene cover layer; and
- 8 - Printable with ink, stroke widths down to 0.1mm.

- 15
- 16 Auxiliary coatings or deposited layers on the substrate include:
 - 18 - Local conductive tracking;
 - 19 - Local hydrophobic coatings (e.g. PTFE);
 - 20 - Local hydrophilic coatings (eg titanium oxide); and
 - 21 - Bio-compatible coatings (e.g. parylene).

- 22
- 23 The seal 192 may be a single or composite layer but a dual composite construction may be beneficial in that the outer layer can be specified to resist the thermal affects of the heat sealing tool whereas the inner layer is able to melt and create a seal without putting the integrity of the membrane at risk. Properties of the seal layer include:

- 30 - Seal Thickness: Typically in range 10um to 50um;
- 31 - Chemical Resistance: As per substrate above;
- 32 - Optical : As per substrate above;

1 It is preferred that the seal be suitable for penetration
2 by a probe (typically 0.5-1mm diameter) e.g. for liquid
3 delivery or for electrical probing. A self healing or re-
4 sealable penetration hole is preferred.

5

6 Pre-forming of the seal (schematically as in Figures 22
7 and 23) is optional to enhance rigidity of the sealing
8 layer during penetration and to provide the necessary
9 space within the tape for processing materials.

10

11 The carrier layer 193 can comply with EIA-481-B
12 (Electronic Industries Alliance), the standard for
13 "Embossed carrier Taping" for automated component
14 handling in the electronic industries. A preferred
15 material is either black or translucent polystyrene,
16 preferred thickness is in the range 100um to 300um. This
17 layer will be formed prior to assembly of the
18 substrate/cover such that the substrate/cover will be
19 contained within a recessed channel in the carrier tape
20 and thereby avoid contact with any other surfaces during
21 manufacture or distribution (e.g. in a reel), or at point
22 of use.

23

24 The primary functions of the carrier layer are a) to
25 provide a mechanically robust carrier for the more
26 fragile substrate/cover layers b) incorporate punched
27 holes which provide a means of transport drive for the
28 tape c) incorporate registration features which align the
29 substrate/cover layer with the punched drive holes d)
30 incorporate apertures which allow the channels in the
31 substrate to be visible from underneath the tape.

32

1 With reference to Figure 20, which is a section across
2 the width of the tape, not to scale, a 50um thick
3 microfluidic substrate 201 formed up to 250um deep, is
4 contained within the 300um thickness of the carrier 202
5 thus affording it protection. The substrate has analyte
6 203 and is capped with the seal 204.

7

8 With reference to Figure 21, a negative pressure (vacuum)
9 is applied to the two ports 210 that distorts the
10 substrate onto a tool 211 such as a viewing window of a
11 scanner or a heating/cooling plate.

12

13 With reference to Figure 22, a sample loading probe 221
14 is positioned ready to penetrate a reservoir in the pre-
15 formed cover seal 222 (that is dimpled for ease of
16 insertion). The substrate contains analyte 223 and the
17 reservoir contains electrolyte 224.

18

19 With reference to Figure 23, electrokinetics 231 probes
20 are shown penetrating the reservoirs.

21

22 With reference to Figure 24, probes 241 external to the
23 "wet chemistry" zone are shown connecting to conductive
24 layers on the substrate that are an anode 242 and a
25 cathode 243.

26

27 For the preferred embodiment, a single segment of tape
28 will be described below, comprising the means of
29 processing one discrete test sample of bio-material such
30 as DNA.

31

32 Figure 25 shows a supporting layer 251 comprises a thin
33 flat optically clear film of either polycarbonate,

1 polyester, polystyrene, poly methyl methacrylate, or
2 other co-polymers of these materials. This film will
3 typically be 125um thick but other thicknesses in the
4 range 25um to 1000um may be used. This Layer has a
5 pattern of conductive tracks 252 and 253 applied by
6 screen printing or laser printing or ink jet printing as
7 well as a pattern 254 which can be machine read to
8 indicate the identity of that segment.

9

10 Figure 26 shows a formed patterned layer 265 comprising a
11 thin film of either polycarbonate, polyester,
12 polystyrene, polyethylene, polymethyl methacrylate,
13 polypropylene or other co-polymers of these materials.
14 This film will be typically 50um thick but other
15 thicknesses in the range 10um to 200um may be used. This
16 material need not be optically transparent and some
17 advantage may be gained by having it translucent or
18 opaque; translucency offers a means of back-lighting
19 scatter (opposite side from the optical supporting layer)
20 which may be used for illuminating and capturing an image
21 of the tape processes; opaqueness offers the possibility
22 of using a reflected front-lighting source.

23

24 High pressure thermoforming is preferably used to create
25 formed cavities 266, connecting channels 267, optional
26 side channels 268, primary access ports 269 and secondary
27 optional access ports 2610 . Shallow channels 2611
28 provide entry slots for the conductive tracks 252, 253.
29 Typical relative depths of these formed features is
30 illustrated in typical section Figure 31.

31

32 Figure 27 shows a further preparative step in
33 manufacturing the formed patterned layer whereby a

1 knifing or blanking process is used to cut apertures or
2 slots in the film. Apertures 2712 provide the access
3 entry slots for the conductive tracks 252, 253. Aperture
4 2713 ensures that the code mark 254 is not obscured by
5 any translucency or opaqueness in the film 265.

6

7 Figure 28 shows layer 251 and layer 265 assembled
8 together. This will be effected by either a heat sealing
9 or an adhesive process or both, to ensure that the two
10 layers achieve a tight seal around the profile of the
11 various patterned recesses 266, 267, 2611 etc. in Layer
12 265. Heat sealing can be achieved by the contact surface
13 material of Layer 265 comprising a thin layer of low
14 melting point polymer such as poly-ethylene;
15 alternatively adhesive bonding can comprise the use of
16 commercial cyano-acrylate or, in the case of sealing
17 zones 2814, a commercial silicone rubber compound may be
18 used.

19

20 Figure 29 shows an exoskeleton component 2915 whose
21 purpose is to protect layer 265 as well as providing
22 rigid access ports 2916, 2917 for loading and unloading
23 the tape. Apertures 2918 protect the cavities 266 and an
24 aperture 2919 protects the channel 267.

25

26 The exoskeleton material is preferably a rigid polymer
27 such as polycarbonate, ABS, polyester, polystyrene,
28 polyethylene, polymethyl methacrylate, polypropylene or
29 other co-polymers of these materials. This exoskeleton
30 will be typically 1.0mm thick but other thicknesses in
31 the range 0.5mm to 3mm may be used.

32

1 Figure 30 shows the rigid exoskeleton 2915 affixed to the
2 layer 251 plus layer 265 assembly. This may be by
3 adhesive bonding or by incorporating protrusions in the
4 exoskeleton 2915 which will snap fit into corresponding
5 apertures in the supporting layer 251. Where the Layer
6 265 adjoins an access port on the exoskeleton 2915, for
7 example, at cavity locations 3021, an adhesive layer,
8 preferably a commercial silicone rubber compound, will
9 ensure intimate local contact between Layer 265 and
10 exoskeleton 2915.

11

12 Figure 31 shows a section 3100 through the assembly 3101
13 along the line "D" to "D". Depths are exaggerated in this
14 figure for clarity, but a typical overall height of the
15 exoskeleton is 1mm. This cross section shows that
16 cavities 266 are raised to the height of the exoskeleton,
17 cavities 269 are raised to a lesser extent (typically
18 0.5mm) and the channel 267 has a low profile (typically
19 50 to 200um deep). A conductive strip 253 (typically 20
20 to 50um thick) is shown entering a cavity 256. Sealing
21 plugs 3124 are shown at the access port locations. These
22 sealing plugs will comprise compliant polymer, preferably
23 an elastomer such as polyurethane or silicone rubber.
24 These plugs will incorporate a feature allowing removal
25 and replacement by a simple hand tool or, for continuous
26 unattended operation, allow automated removal and
27 replacement. Note also feature 3123 which is a tapered
28 section of cavity forming a smooth transition between the
29 cavity 266 and the channel 267.

30

31 Figure 32 shows a method of loading liquid electrolyte
32 (for example 2mM Tris, 2mM Acetate, 0.5mM EDTA) by
33 accessing a probe 3225 into an end cavity. Locations 3226

1 may be vented and sealed (plugs 3124) as part of the
2 filling process. Note that the micro-scale of the
3 penetration points will allow surface tension to prevent
4 unwarranted leakage while the sealing caps are applied.
5

6 Figure 33 shows a method of pre-loading a column of gel
7 3328 at the point of manufacture using a loading probe
8 3327. The gel is loaded as a pre-determined dispensed
9 volume from the elution cavity end of the test segment.
10 The gel is preloaded with a fluorescing marker dye.
11

12 The test segment has now been pre-loaded ready for use,
13 and will be shipped in this condition to the point of
14 use. The only "wet chemistry" at the point of use is to
15 load the test sample for analysis.
16

17 Figure 34 shows a loading probe 3429 penetrating through
18 the top loading port of the exoskeleton at the point of
19 use. The corresponding cap 3124 may be discarded or
20 replaced depending on whether the tape is required to be
21 archived after use. The test sample 3430 will be prepared
22 in a solution which is denser than the surrounding
23 electrolyte in the tape cavity, for example, a solution
24 of sucrose will ensure that the test sample will flow
25 under gravity into the tapered channel and gather right
26 at the top of the gel column.
27

28 The exoskeleton incorporates access ports which can be
29 oriented longitudinally (e.g. port no. 3431) or
30 perpendicularly (e.g. port no. 3432). Optionally port
31 3432 can be used to vent any unwanted build up of gas in
32 the lower cavity.
33

1 These fabrication methods can create features which
2 provide a wide range of processing options at the point
3 of use.

4

5 With reference to Figure 35, the automated processing has
6 the steps of transporting the tape and selecting an area
7 for processing 351, piercing the apparatus with a probe
8 or probing the apparatus 352, and performing microfluidic
9 processing 353 at the selected area, then repeating 354
10 the above steps until processing of the reel of tape is
11 complete.

12

13 During these steps the fabricated apparatus with its
14 optional preloaded processing materials may be deformed
15 in order to cause dynamic processing. The apparatus may
16 be deformed by bending, flexing, folding, twisting,
17 conforming to a rigid surface, mechanical deformation,
18 deformation by applying a sound pressure, deformation by
19 applying a liquid pressure, and deformation by applying a
20 gas pressure. Optionally the deformation can result in
21 the bringing of a part of the apparatus back into contact
22 with another part of itself or with another apparatus.

23 The deformation may move part of the apparatus into a
24 position for processing, including being in contact with
25 a processing tool. The deformation of the apparatus
26 results in dynamic processing that includes pumping,
27 filling, pouring, pressurising, mixing, dispensing,
28 aspirating, separating, combining, heating and cooling.

29

30 Apparatuses that include impermeable membranes facilitate
31 further novel processing methods that involve the
32 impermeable membrane. The membrane may be pierced by one
33 or more probes. These probes may be pipettes.

1 Conducting probes that have pierced the membrane may
2 provide an electrical potential, and used for passing an
3 electric current through the conducting probe into a
4 conducting medium.

5

6 Optionally a grid of probes are mounted on a discrete
7 carrier or a continuous carrier that can be indexed or
8 replaced, such that another set of probes can be used
9 after the first set has worn out.

10

11 The grid of probes may be configured such that each probe
12 is separately addressable and each probe may have a
13 separate voltage applied in order to progressively move
14 the processing material through processing elements, such
15 as indented troughs and permeation layers in the
16 apparatus; after the grid of probes has penetrated or
17 contacted a corresponding grid of impermeable membranes.

18 This arrangement can be used to move process materials
19 through permeation layers for molecular separation. The
20 controlled and progressive switching of voltages on the
21 grid of probes can be used to split processing material
22 into more than one separate processing path through more
23 than one separate processing elements. These split
24 process materials may be further combined or different
25 process materials may be combined at the junctions of
26 paths through the apparatus. In this way, the grid of
27 electrical probes can be configured to apply voltages
28 that cause a multi-dimensional separation of molecules,
29 e.g. polypeptide or protein molecules.

30

31 If the probes are pipettes, processing materials may be
32 introduced into the apparatus through the impermeable
33 membranes that have been penetrated or processing

1 materials removed from within the apparatus. An array of
2 pipettes compatible with 96, 192, 384, 1536 or 3456 well
3 assay plates can be matched to an array of commensurately
4 spaced impermeable membranes for penetration by the array
5 of pipettes. Probes that penetrate or touch the surface
6 of a membrane can cause processing to be performed, such
7 as pumping, filling, pouring, pressurising, mixing,
8 dispensing, aspirating, separating, combining, heating,
9 cooling, movement by electrokinesis, movement by
10 electrokinesis, movement by the molecular entrapment
11 method of molecular tweezers, acoustic tweezers and bio-
12 molecular motor principles.

13

14 An apparatus in the form of a tape may be transported
15 through processing equipment and handling equipment by
16 friction of, for example, rollers in contact with the
17 apparatus or by pinions inserted into indents or
18 perforations in the apparatus in a similar manner to the
19 handling of photographic or cine film. Alternative
20 methods of moving the tape include sliding drawers and
21 walking beams. Moving the apparatus with electromagnetic
22 fields and induction within the apparatus or moving using
23 air or fluid pressure applied to the apparatus are also
24 possible.

25

26 The position of the apparatus in response to movement is
27 detected by measurement of indexing patterns. After
28 movement dynamic processing can be performed and then
29 further repeated movement and dynamic processing steps
30 can be performed in a continuous fashion as the
31 continuous tape is indexed through the processing
32 equipment.

33

1 In conclusion, we present the advantages of the present
2 invention.

3

4 A significant and long-established traditional art for
5 some of the kinds of bio-molecular separation described
6 herein is commonly referred to as "slab gel
7 electrophoresis". The demands in material usage, process
8 time, operator time and workspace for this process are
9 recognised by those with even minor experience of this
10 art. The procedure commonly employs manual preparation of
11 gels involving mixing, heating and casting steps.

12 Although the method can now employ pre-cast gels to
13 provide some degree of improvement, the overall process
14 remains manually intensive and inefficient.

15

16 In contrast, the present invention offers significant
17 advantages, by miniaturising all the elements of this
18 traditional process and eliminating many of the material
19 preparation and manual processing tasks.

20

21 While the traditional processes remain in common use, new
22 art is emerging which includes miniaturised bio-analysis
23 systems employing chip-scale technology, micro-fluidics,
24 and semiconductor fabrication techniques.

25

26 The present invention provides advantages over both
27 traditional and emerging techniques.

28

29 The present invention provides very significant savings
30 in materials, time and workspace over traditional gel
31 electrophoresis methods.

32

1 The present invention provides an adaptable platform for
2 a very wide range of bio-analysis processes (not just gel
3 electrophoresis) and employs geometric patterning,
4 tooling methods and fabrication methods which are much
5 less complex than other emerging micro-fluidic or chip
6 scale techniques. This allows rapid and cost effective
7 production of multiple versions of tape to match the
8 range of applications anticipated.

9

10 The present invention allows bio-sample processing in a
11 range from one single simple test up to highly parallel
12 and multiple complex tests in an uninterrupted continuous
13 serial or parallel mode. The former is attractive to
14 small research laboratories, many quality control
15 laboratories, and point of care clinics. The latter is
16 attractive to high throughput processing laboratories. A
17 combination of these processing methods is attractive to
18 public health hospitals and clinics whose demand can
19 fluctuate significantly. This range of capability is
20 provided in one single effective and efficient platform
21 regardless of usage patterns.

22

23 The present invention configures processing elements on a
24 highly flexible substrate and enables a versatile range
25 of substrate indexing patterns and transport methods to
26 be utilised as described.

27

28 Additionally, these transport methods provide the
29 advantage of allowing the use of non complex, compact,
30 low cost optical scanning means by the embodiment of a
31 fixed position transverse optical line-scanning system
32 whose focal plane is along a line across the width of the

1 substrate. The scanning function is provided by the
2 (already provided) indexing motion of the substrate.

3

4 This highly flexible substrate also enables the other
5 described features and advantages which result from
6 bending, folding, twisting, flexing and deforming its
7 geometry.

8

9 The substrate flexibility also allows it to be penetrable
10 by probes for the purposes of processing material
11 delivery or removal, electrical connection and process
12 tooling introduction.

13

14 Additionally this flexible substrate is suitable for
15 affixing a secondary impermeable membrane which is also
16 readily penetrable by suitable probes for the purposes of
17 processing material delivery or removal, electrical
18 connection, process tooling introduction.

19

20 The penetrable substrate and penetrable membrane provides
21 a processing system which can be fully enclosed and which
22 can provide some processing materials pre-loaded within
23 the system. This minimises preparation, avoids spillage,
24 avoids the need for cleaning or flushing procedures and
25 simplifies waste disposal.

26

27 Alternatively, a stereo-lithographic method is described
28 to fabricate the substrate and the impermeable membrane
29 in one homogenous material with the advantage that this
30 simplifies the means of construction.

31

32 Alternatively, a selective laser sintering method is
33 described to fabricate the substrate and the impermeable

1 membrane in a single fabrication process again with the
2 advantage that this simplifies the means of construction.
3

4 The present invention employs one generic material type
5 in its construction (polymer) and avoids the significant
6 use of glass, silicon or metal in its fabrication. This
7 simplifies the waste disposal methods after bio-
8 processing is complete.

9

10 The fabrication techniques described provide a wide range
11 of substrate geometries. These features can be created
12 by rapid and simple methods of tooling, thus avoiding the
13 long lead times and complexity of other miniaturised bio-
14 processing systems.

15

16 The present invention has the advantage that these rapid
17 and simple fabrication techniques correspond to
18 processing elements whose dimensional accuracy is less
19 critical than those of chip scale devices. A
20 corresponding advantage is that this is achieved without
21 sacrifice to the overall device size because the device
22 size, in the current state of the art, is determined by
23 the practicalities of the size of the sample loading
24 wells and not by the processing element sizes.

25

26 The present invention can be enhanced by pre-printing
27 processing materials onto a planar plastic film substrate
28 using commercially available printing methods and then by
29 deforming that substrate in a non planar fashion such
30 that the pre-printed material deforms into a desired
31 shape or position and such that, for example, a pre-
32 printed permeation layer can subsequently (after forming
33 of the substrate) be hydrated into its gelatinous phase.

1 Related printing and forming methods are already
2 established in the field of foil manufacture for "in-
3 mould decoration" of plastic injection moulded products
4 (used for cosmetic effect mainly on consumer electronic
5 products), but the present invention provides the scope
6 for adapting these methods into this unconnected field of
7 application.

8

9 The flexible substrate is readily available in a range of
10 polymer materials whose optical properties can be matched
11 to available commercial optical systems for detection or
12 imaging of the bio-processing events during system
13 operation.

14

15 Further modifications and improvements may be added
16 without departing from the scope of the invention herein
17 described.

1 CLAIMS

2

3 1. An apparatus for microfluidic processing
4 applications, wherein said microfluidic processing
5 is performed on a selected area of a plurality of
6 areas each individually selectable on said
7 apparatus, characterised in that the apparatus is
8 non-rigid.

9

10 2. An apparatus for mass transport microfluidic
11 processing applications, characterised in that the
12 apparatus is non-rigid.

13

14 3. The apparatus of any previous Claim, wherein said
15 apparatus is a tape.

16

17 4. The apparatus of any previous Claim, wherein said
18 apparatus comprises a polymer film.

19

20 5. The apparatus of any previous Claim, wherein said
21 apparatus comprises processing elements for
22 microfluidic processing.

23

24 6. The apparatus of Claim 5, wherein said processing
25 elements comprise indents of said apparatus.

26

27 7. The apparatus of any of Claims 5 to 6, wherein said
28 processing elements comprise cavities embedded
29 within said apparatus.

30

31 8. The apparatus of any of Claims 5 to 7, wherein said
32 processing elements comprise processing materials in
33 intimate contact with the surface of said apparatus.

- 1
- 2 9. The apparatus of any of Claims 5 to 8, wherein said
- 3 processing elements comprise processing materials
- 4 embedded within said apparatus.
- 5
- 6 10. The apparatus of any of Claims 5 to 9, wherein said
- 7 processing elements comprise opaque, translucent or
- 8 coloured materials for providing optical isolation
- 9 between elements or providing indexing marks.
- 10
- 11 11. The apparatus of any previous Claim, wherein an
- 12 element of said apparatus is transparent.
- 13
- 14 12. The apparatus of any previous Claim, wherein said
- 15 apparatus is penetrable.
- 16
- 17 13. The apparatus of Claim 12, wherein said apparatus is
- 18 self sealing during penetration.
- 19
- 20 14. The apparatus of Claims 12 to 13, wherein said
- 21 apparatus is self sealing after penetration.
- 22
- 23 15. The apparatus of any previous Claim, wherein said
- 24 apparatus further comprises an impermeable membrane.
- 25
- 26 16. The apparatus of Claim 15, wherein said impermeable
- 27 membrane is affixed in intimate contact with parts
- 28 of the surface of said apparatus.
- 29
- 30 17. The apparatus of any of Claims 15 to 16, wherein
- 31 said impermeable membrane is arranged as discrete
- 32 areas of impermeable membrane in intimate contact
- 33 with parts of the surface of said apparatus.

- 1
- 2 18. The apparatus of any of Claims 15 to 17, wherein
- 3 said impermeable membrane is penetrable.
- 4
- 5 19. The apparatus of any of Claims 15 to 18, wherein
- 6 said impermeable membrane is self sealing during
- 7 penetration.
- 8
- 9 20. The apparatus of any Claims 15 to 19, wherein said
- 10 impermeable membrane is self sealing after
- 11 penetration.
- 12
- 13 21. The apparatus of any Claims 15 to 20, wherein said
- 14 impermeable membrane is re-sealed by a capping
- 15 element after penetration.
- 16
- 17 22. The apparatus of any Claims 15 to 21, wherein said
- 18 impermeable membrane is supported by support
- 19 structures.
- 20
- 21 23. The apparatus of any previous Claim, wherein said
- 22 apparatus further comprises a non-rigid member.
- 23
- 24 24. The apparatus of Claim 23, wherein said non-rigid
- 25 member is affixed in intimate contact with parts of
- 26 the surface of said apparatus.
- 27
- 28 25. The apparatus of any of Claims 23 to 24, wherein
- 29 said non-rigid member is arranged as discrete areas
- 30 of non-rigid member in intimate contact with parts
- 31 of the surface of said apparatus.
- 32

- 1 26. The apparatus of any of Claims 23 to 24, wherein
2 said non-rigid member is penetrable.
3
- 4 27. The apparatus of any of Claims 23 to 26, wherein
5 said non-rigid member is self sealing during
6 penetration.
7
- 8 28. The apparatus of any of Claims 23 to 27, wherein
9 said non-rigid member is self sealing after
10 penetration.
11
- 12 29. The apparatus of any of Claims 23 to 28, wherein
13 said non-rigid member is re-sealed by a capping
14 element after penetration.
15
- 16 30. The apparatus of any of Claims 23 to 29, wherein
17 said non-rigid member is supported by support
18 structures.
19
- 20 31. A method of fabrication of an apparatus for mass
21 transport microfluidic processing applications
22 comprising the step of forming an apparatus that is
23 non-rigid.
24
- 25 32. A method of fabrication of an apparatus for mass
26 transport microfluidic processing applications
27 comprising the step of fabricating a tape.
28
- 29 33. The method according to any of Claims 31 to 32,
30 wherein said step of forming said apparatus
31 comprises the step of high pressure plastic film
32 forming with said high pressure acting on said
33 apparatus.

1

2 34. The method of Claim 33, wherein said step of high
3 pressure plastic film forming is arranged with the
4 high pressure acting on a compliant membrane, which
5 is part of the forming tool in contact with said
6 apparatus.

7

8 35. The method of any of Claims 31 to 34, wherein said
9 step of fabricating said apparatus further comprises
10 the step of preloading processing materials onto
11 said apparatus before fabrication.

12

13 36. The method of any of Claims 31 to 34, wherein said
14 step of fabricating said apparatus further comprises
15 the step of loading processing materials onto said
16 apparatus during fabrication.

17

18 37. The method of Claim 36, wherein said step of
19 preloading or loading during fabrication of said
20 apparatus comprises the step of depositing
21 processing materials onto a carrier.

22

23 38. The method of Claim 36, wherein said step of
24 preloading or loading during fabrication of said
25 apparatus comprises the step of depositing
26 processing material onto a non-rigid member.

27

28 39. The method of any of Claims 36 to 38, wherein said
29 deposited processing material comprises permeation
30 layers.

31

- 1 40. The method of any of Claims 36 to 39, wherein said
2 deposited processing material comprises conductive
3 material.
- 4
- 5 41. The method of any of Claims 36 to 40, wherein said
6 deposited processing material comprises chemically
7 or biologically active material.
- 8
- 9 42. The method of any of Claims 36 to 41, wherein said
10 deposited processing material comprises marks for
11 identity purposes.
- 12
- 13 43. The method of any of Claims 36 to 42, wherein said
14 deposited processing material comprises magnetisable
15 material.
- 16
- 17 44. The method of any of Claims 36 to 43, wherein said
18 step of depositing comprises printing.
- 19
- 20 45. The method of Claim 36, wherein said step of
21 preloading or loading during fabrication of said
22 apparatus is performed by a loading process selected
23 from a list of processes comprising: deposition and
24 etching, injection into a cavity and injection into
25 an indentation.
- 26
- 27 46. The method of any of Claims 31 to 34, wherein said
28 method of fabrication of said apparatus further
29 comprises the steps of depositing patterns on an
30 apparatus and forming said apparatus, wherein the
31 localised formation of said processing elements is
32 responsive to the distortion by said forming of said
33 deposited pattern.

1

2 47. The method of any of Claims 31 to 34, wherein said
3 method of fabrication of said apparatus further
4 comprises the steps of depositing patterns on an
5 apparatus and localised formation of said apparatus
6 is responsive to the topography of said deposited
7 pattern, resulting in the formation of said
8 processing elements.

9

10 48. The method of any of Claims 46 to 47, wherein said
11 step of depositing comprises pre-printing.

12

13 49. A method of fabrication of an apparatus for mass
14 transport microfluidic processing applications,
15 comprising the step of including an impermeable
16 membrane as part of said apparatus.

17

18 50. The method of Claim 49, wherein said step of
19 including an impermeable membrane comprises the step
20 of affixing an impermeable membrane to a substrate.

21

22 51. The method of any of Claims 49 to 50, wherein said
23 step of including an impermeable membrane comprises
24 the step of depositing, overlaying or affixing
25 discrete areas of impermeable membrane in intimate
26 contact with parts of the surface of said apparatus.

27

28 52. The method of any of Claims 49 to 51, wherein said
29 step of including an impermeable membrane comprises
30 the step of depositing, overlaying or affixing an
31 impermeable membrane on said apparatus and
32 selectively removing areas of said impermeable
33 membrane.

1

2 53. The method of Claim 52 wherein said selected removal
3 of said impermeable membrane is performed by the
4 step of cropping.

5

6 54. A method of fabrication of an apparatus for mass
7 transport microfluidic processing applications,
8 comprising the step of including a non-rigid member
9 as part of said apparatus.

10

11 55. The method of Claim 54, wherein said step of
12 including a non-rigid member comprises the step of
13 affixing a non-rigid member to a substrate.

14

15 56. The method of any of Claims 54 to 55, wherein said
16 step of including a non-rigid member comprises the
17 step of depositing, overlaying or affixing discrete
18 areas of non-rigid member in intimate contact with
19 parts of the surface of said apparatus.

20

21 57. The method of any of Claims 54 to 56, wherein said
22 step of including a non-rigid member comprises the
23 step of depositing, overlaying or affixing a non-
24 rigid member on said apparatus and selectively
25 removing areas of said non-rigid member.

26

27 58. The method of Claim 57, wherein said selected
28 removal of said non-rigid member is performed by the
29 step of cropping.

30

31 59. A method of microfluidic processing, comprising the
32 steps of selecting an area of a plurality of areas
33 of an apparatus and performing microfluidic

1 processing at said selected area, characterised in
2 that said apparatus is non-rigid.
3

4 60. The method of Claim 59, wherein said step of
5 performing microfluidic processing comprises
6 contacting at least one conducting element that
7 connects the exterior of said apparatus to the
8 interior of said apparatus.
9

10 61. The method of Claim 60, further comprising the step
11 of providing an electrical potential to at least one
12 conducting element.
13

14 62. The method of any of Claims 59 to 60, further
15 comprising the step of enabling an electrical
16 current to pass through said least one conducting
17 element.
18

19 63. The method of any of Claims 31 to 62, wherein said
20 apparatus is a tape.
21

22 64. The method of any of Claims 31 to 63, wherein said
23 microfluidic processing is mass transport
24 microfluidic processing.
25

26 65. The method of any of Claims 31 to 64, wherein said
27 microfluidic processing is responsive to the
28 deformation of said apparatus.
29

30 66. The method of Claim 65, wherein said deformation
31 comprises deformation by a step selected from a list
32 of steps comprising: bending, flexing, folding,
33 twisting, conforming to a rigid surface, mechanical

1 deformation, deformation by applying a sound
2 pressure, deformation by applying a liquid pressure,
3 and deformation by applying a gas pressure.

4

5 67. The method of Claim 66, wherein said gas pressure is
6 a negative pressure.

7

8 68. The method of any of Claims 66 to 67, wherein said
9 deformation may further comprise the step of
10 bringing part of said apparatus back into contact
11 with another part of itself.

12

13 69. The method of any of Claims 66 to 67, wherein said
14 step of deformation further comprises the step of
15 bringing a part of said apparatus into contact with
16 another apparatus.

17

18 70. The method of any of Claims 66 to 67, wherein said
19 deformation of said apparatus comprises the step of
20 moving part of said apparatus into a position for
21 processing of said part of said apparatus.

22

23 71. The method of Claim 70, wherein said position for
24 processing is a position with said apparatus in
25 contact with a processing tool.

26

27 72. The method of any of Claims 65 to 71, wherein said
28 microfluidic processing is responsive to said
29 deformation of said apparatus, said microfluidic
30 processing being selected from a list comprising
31 pumping, filling, pouring, pressurising, mixing,
32 dispensing, aspirating, separating, combining,
33 heating and cooling.

- 1
- 2 73. A method of processing for microfluidic processing
- 3 applications, characterised in that the processing
- 4 comprises the step of piercing an impermeable
- 5 membrane.
- 6
- 7 74. The method of Claim 73, wherein said step of
- 8 piercing an impermeable membrane is performed with
- 9 at least one probe.
- 10
- 11 75. The method of Claim 74, wherein said at least one
- 12 probe comprises at least one pipette.
- 13
- 14 76. The method of Claim 74, wherein said method of
- 15 processing further comprises the step of providing
- 16 an electrical potential to at least one conducting
- 17 probe that has pierced said membrane.
- 18
- 19 77. The method of Claim 74, wherein said step of
- 20 processing further comprises the step of enabling an
- 21 electrical current to pass through at least one
- 22 conducting probe that has pierced said membrane.
- 23
- 24 78. A method of processing for microfluidic processing
- 25 applications, characterised in that the processing
- 26 comprises the step of piercing an apparatus.
- 27
- 28 79. The method of Claim 78, wherein said apparatus is
- 29 self sealing during said step of piercing.
- 30
- 31 80. The method of any of Claims 78 to 79, wherein said
- 32 apparatus is self sealing after said step of
- 33 piercing.

1

2 81. The method of Claim 78, wherein said apparatus is
3 re-sealed by a capping element after penetration.

4

5 82. The method of any of Claims 78 to 81, wherein said
6 step of piercing the apparatus is performed with at
7 least one probe.

8

9 83. The method of Claim 82, wherein said at least one
10 probe comprises at least one pipette.

11

12 84. The method of Claims 82 to 83, wherein said method
13 of processing further comprises the step of
14 providing an electrical potential to at least one
15 conducting probe that has pierced said apparatus.

16

17 85. The method of Claims 82 to 84, wherein said step of
18 processing further comprises the step of enabling an
19 electrical current to pass through a conducting
20 probe that has pierced said apparatus.

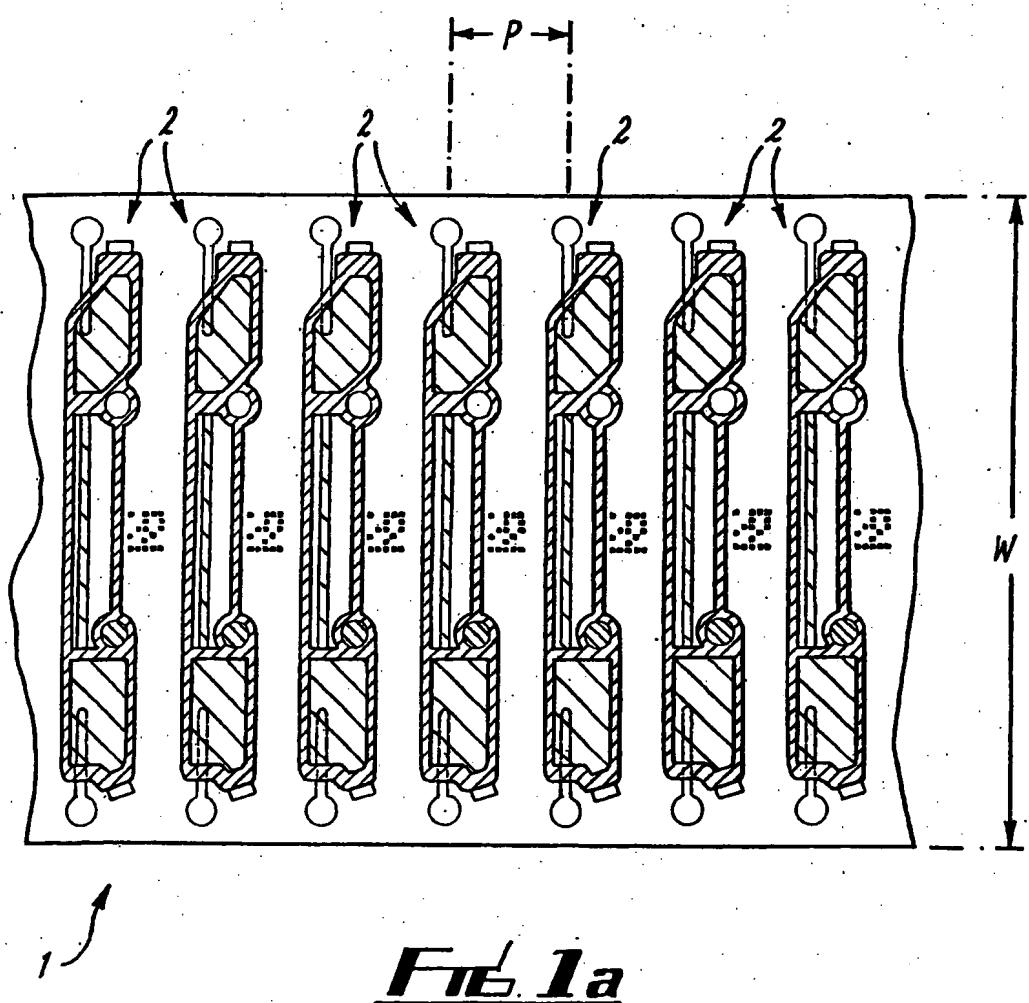
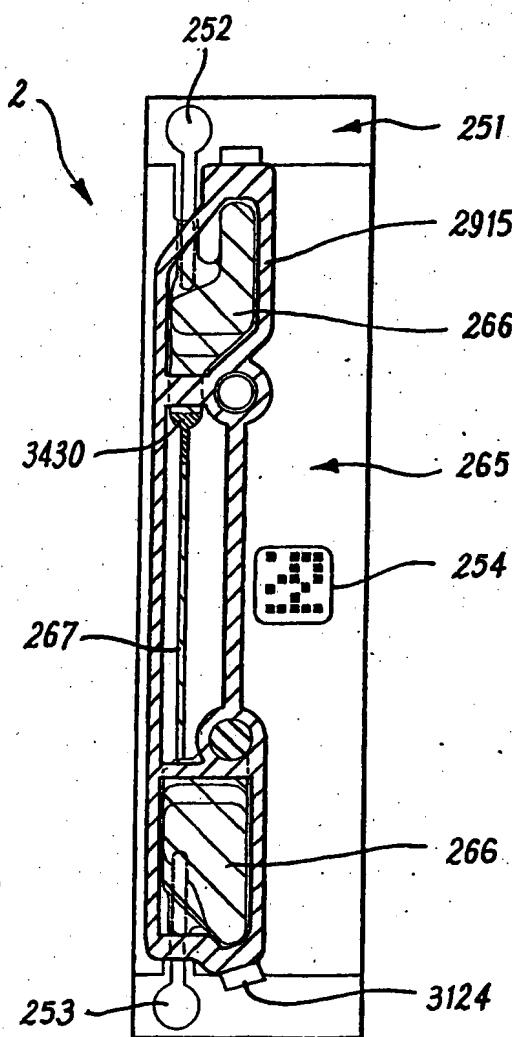


Fig 1a



Fred. Ib

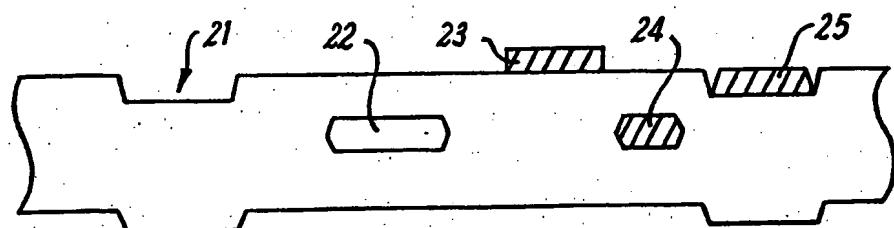


Fig. 2a

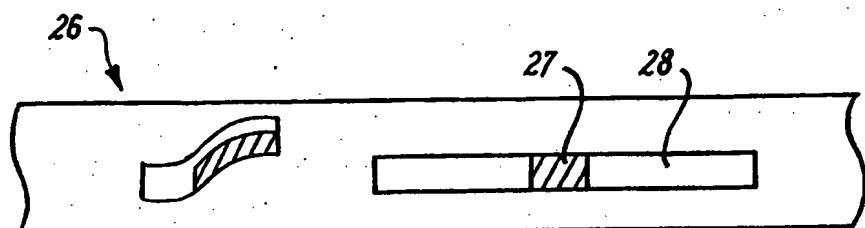


Fig. 2b

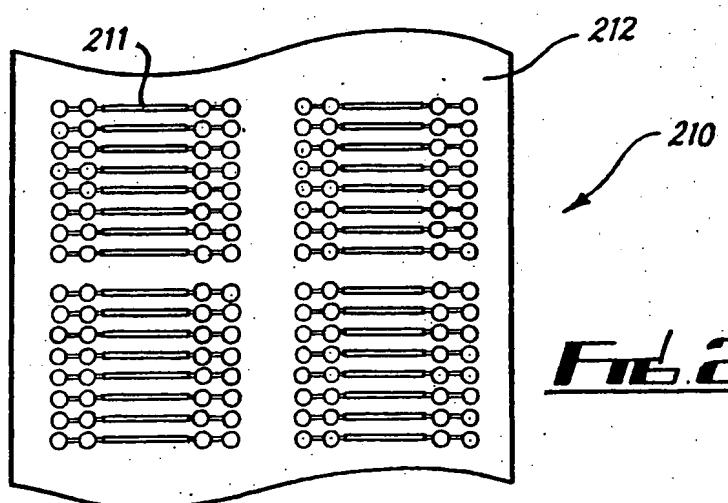


Fig. 2c

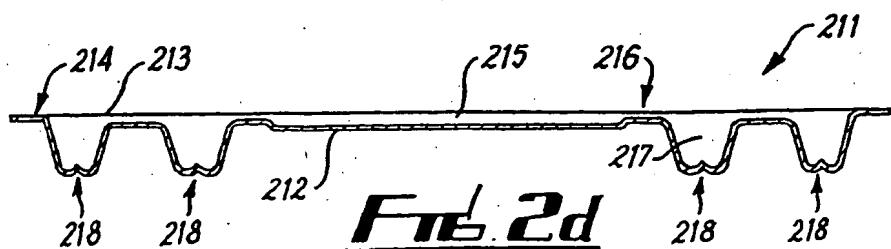


Fig. 2d

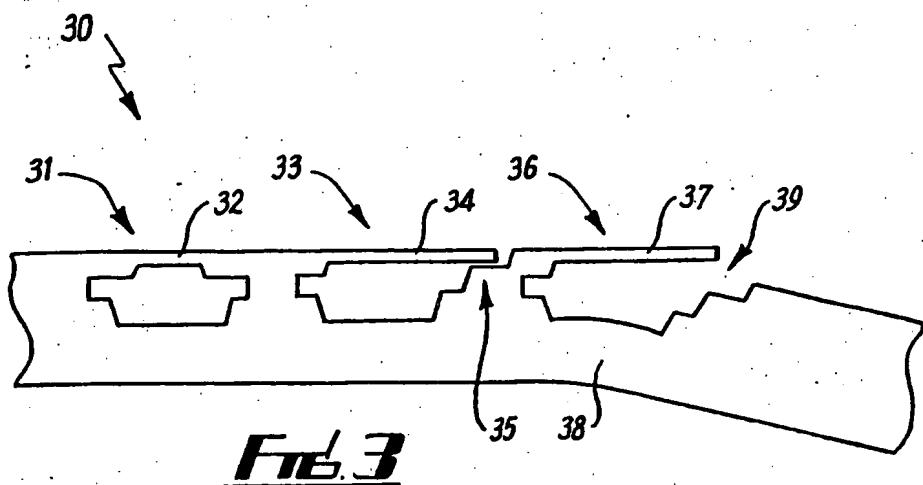


FIG. 3

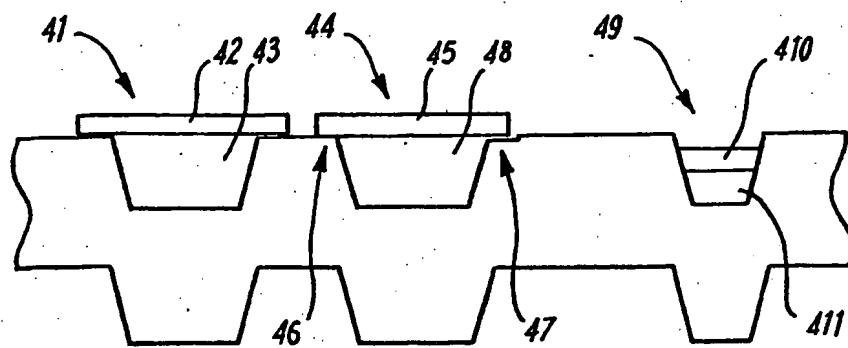


FIG. 4a

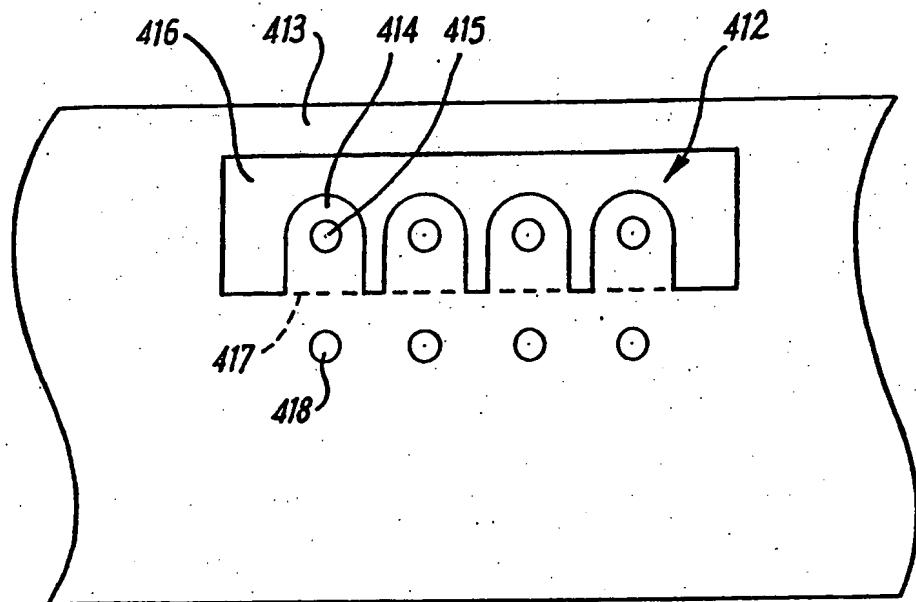


Fig. 4b

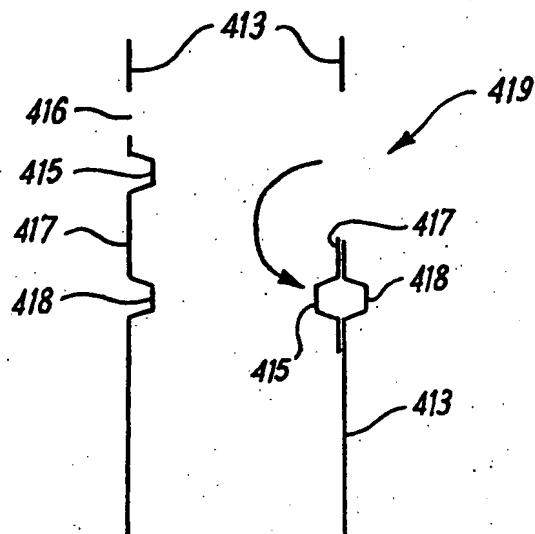
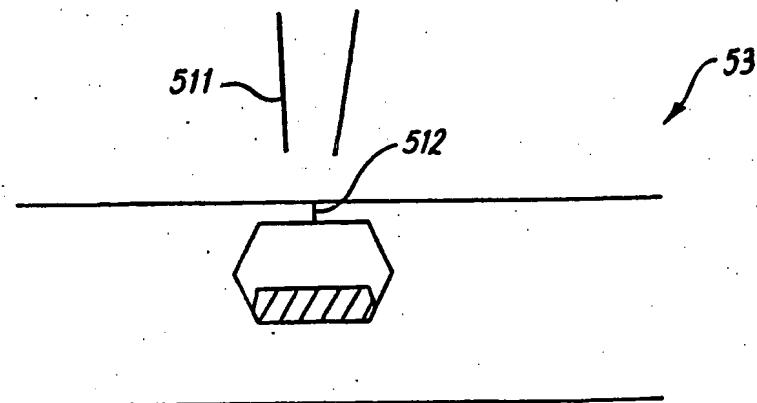
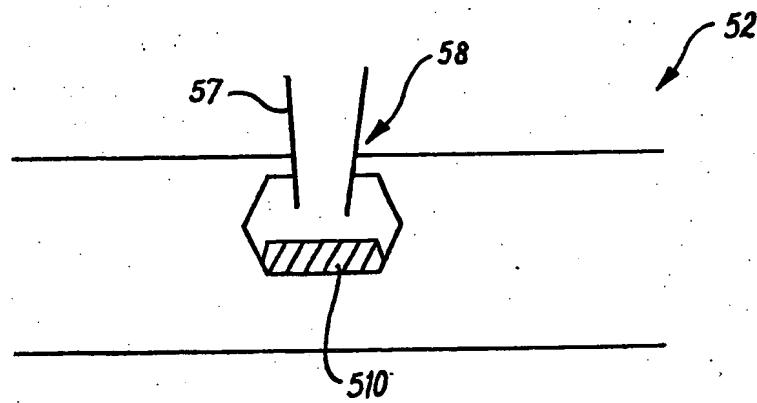
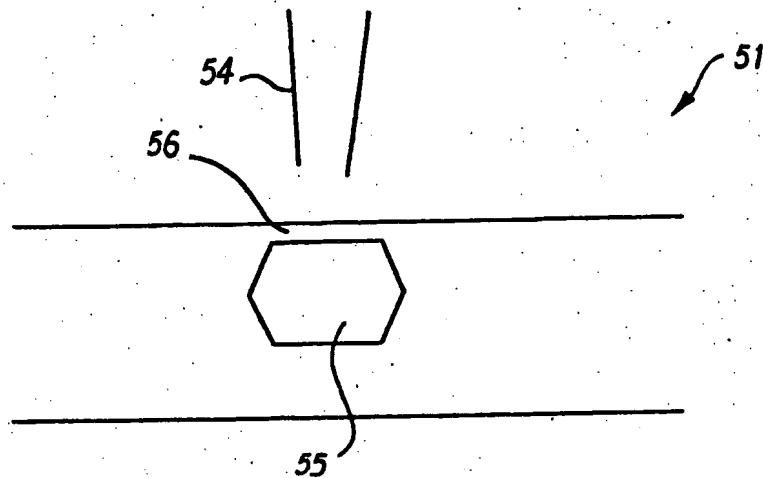
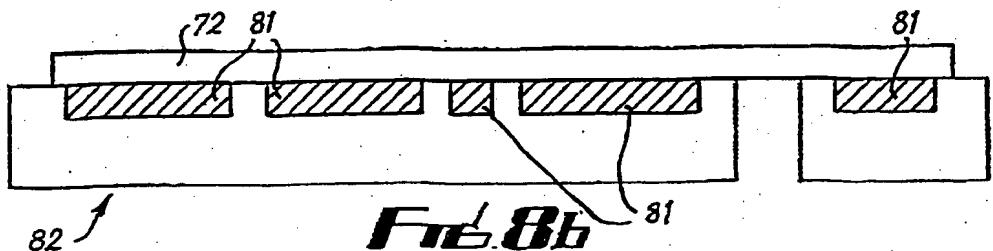
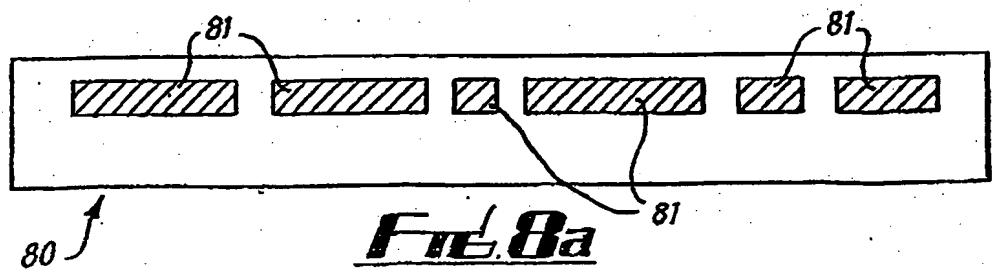
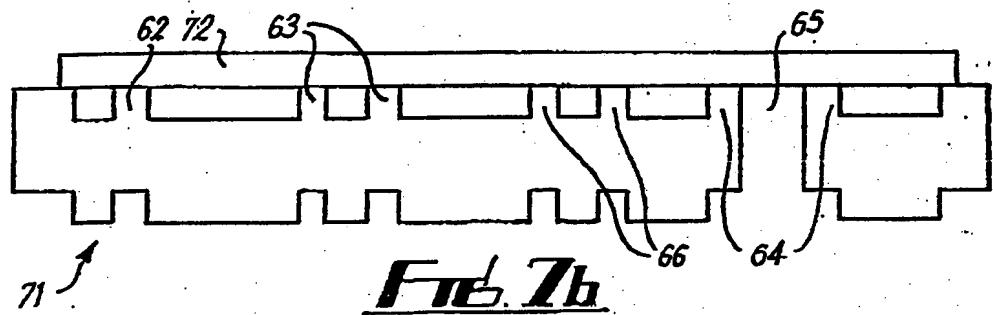
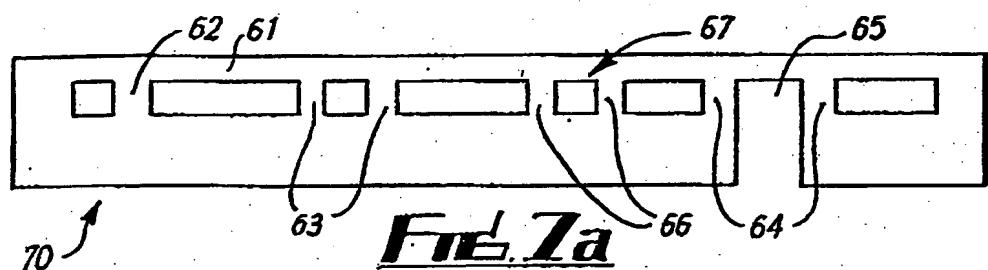
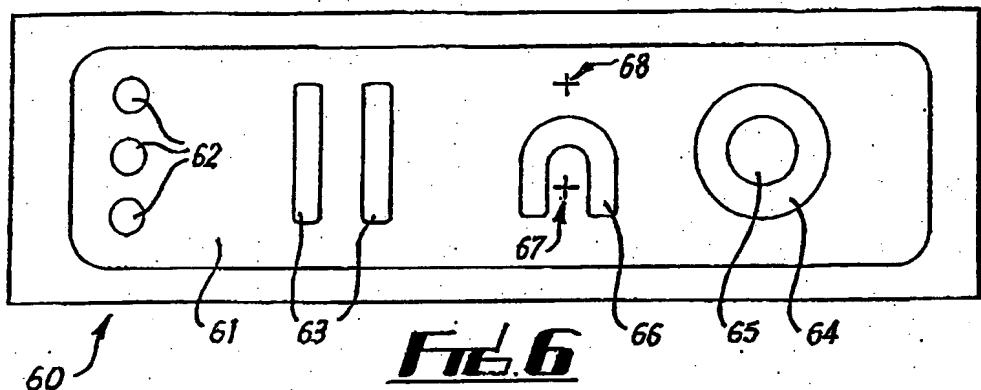


Fig. 4c



Figs

SUBSTITUTE SHEET (RULE 26)



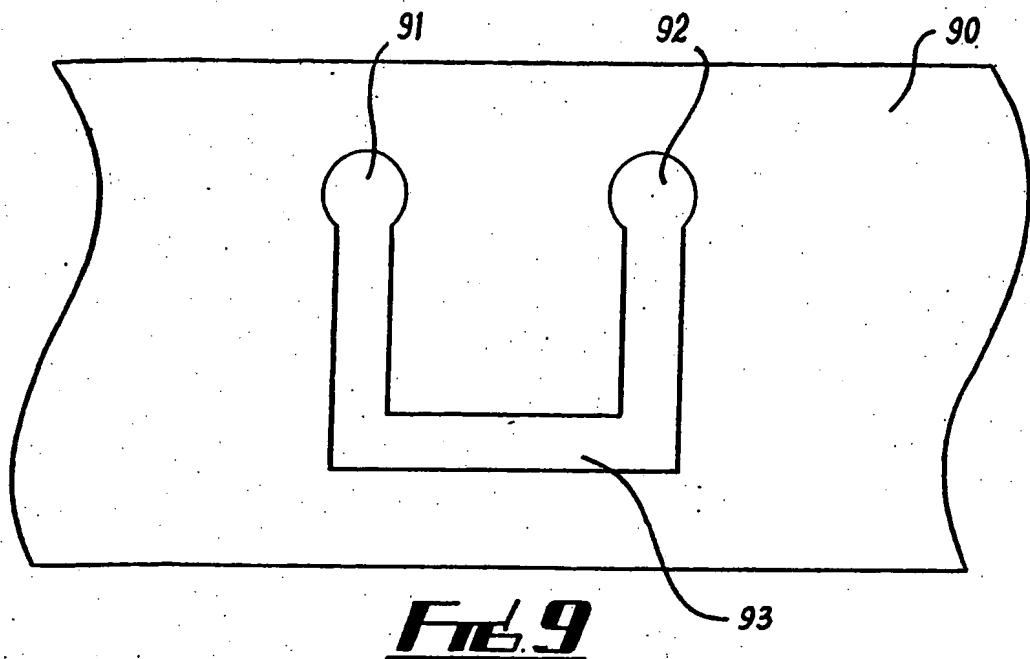


FIG. 9

93

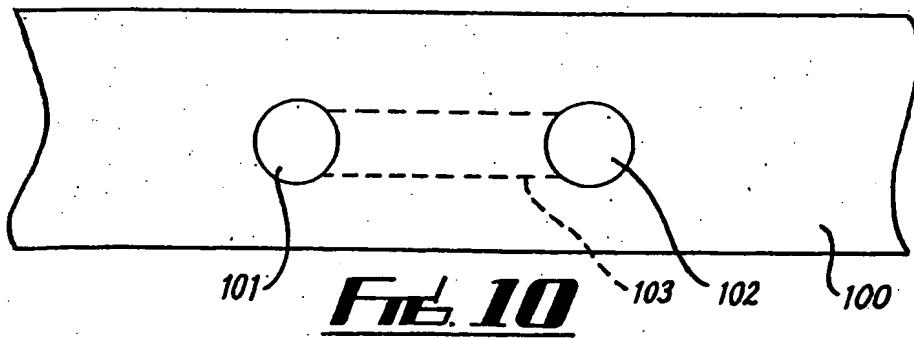


FIG. 10

103

102

100

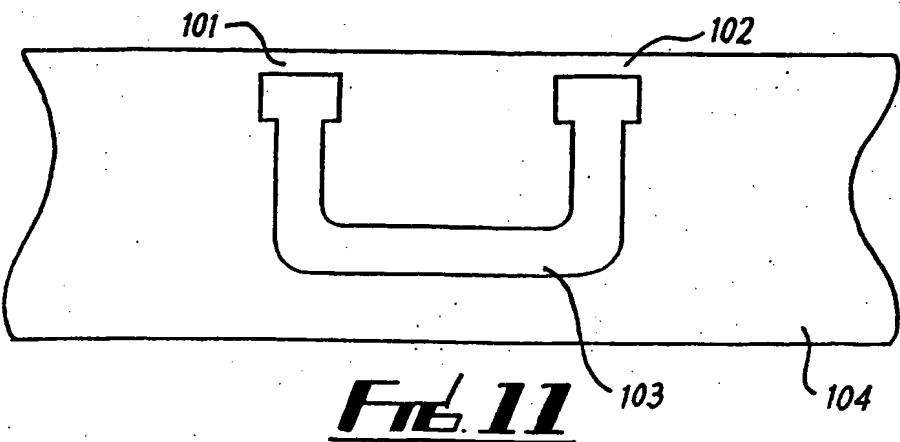
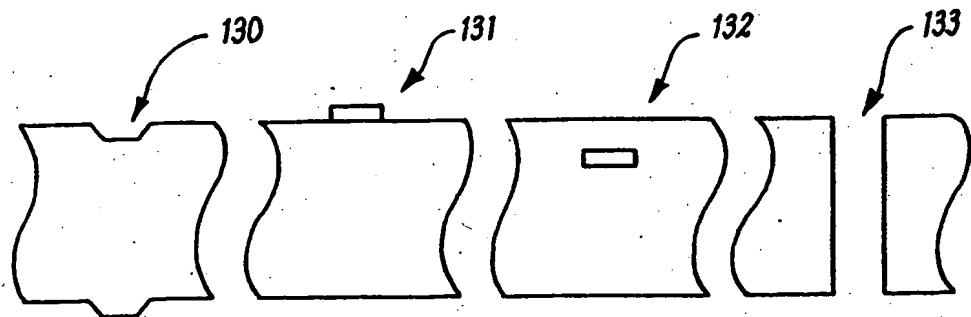
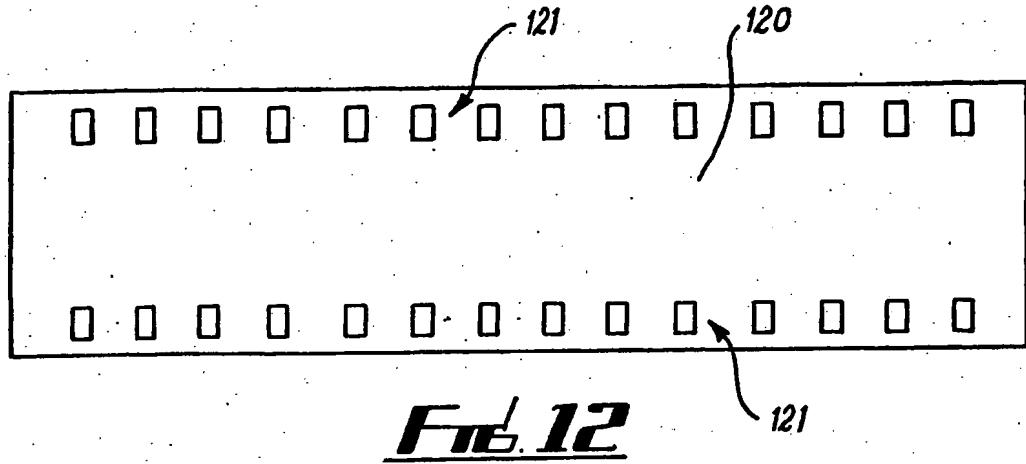


FIG. 11

103

104



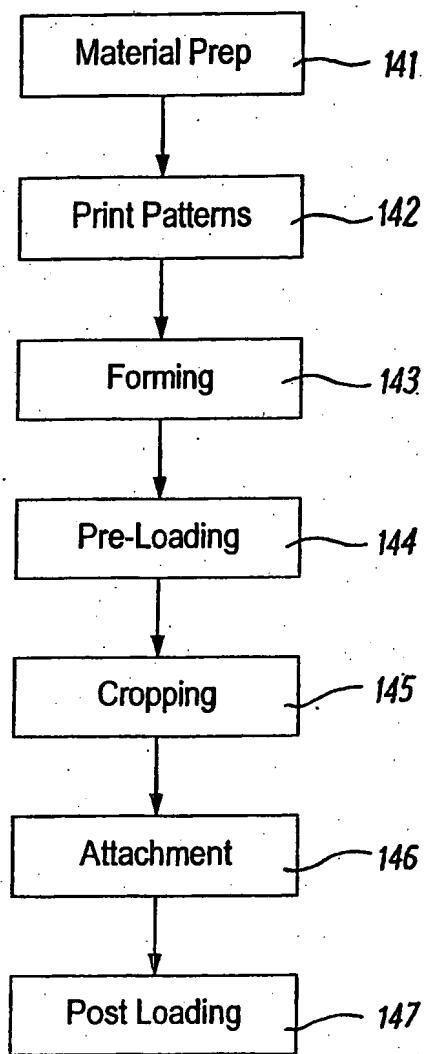
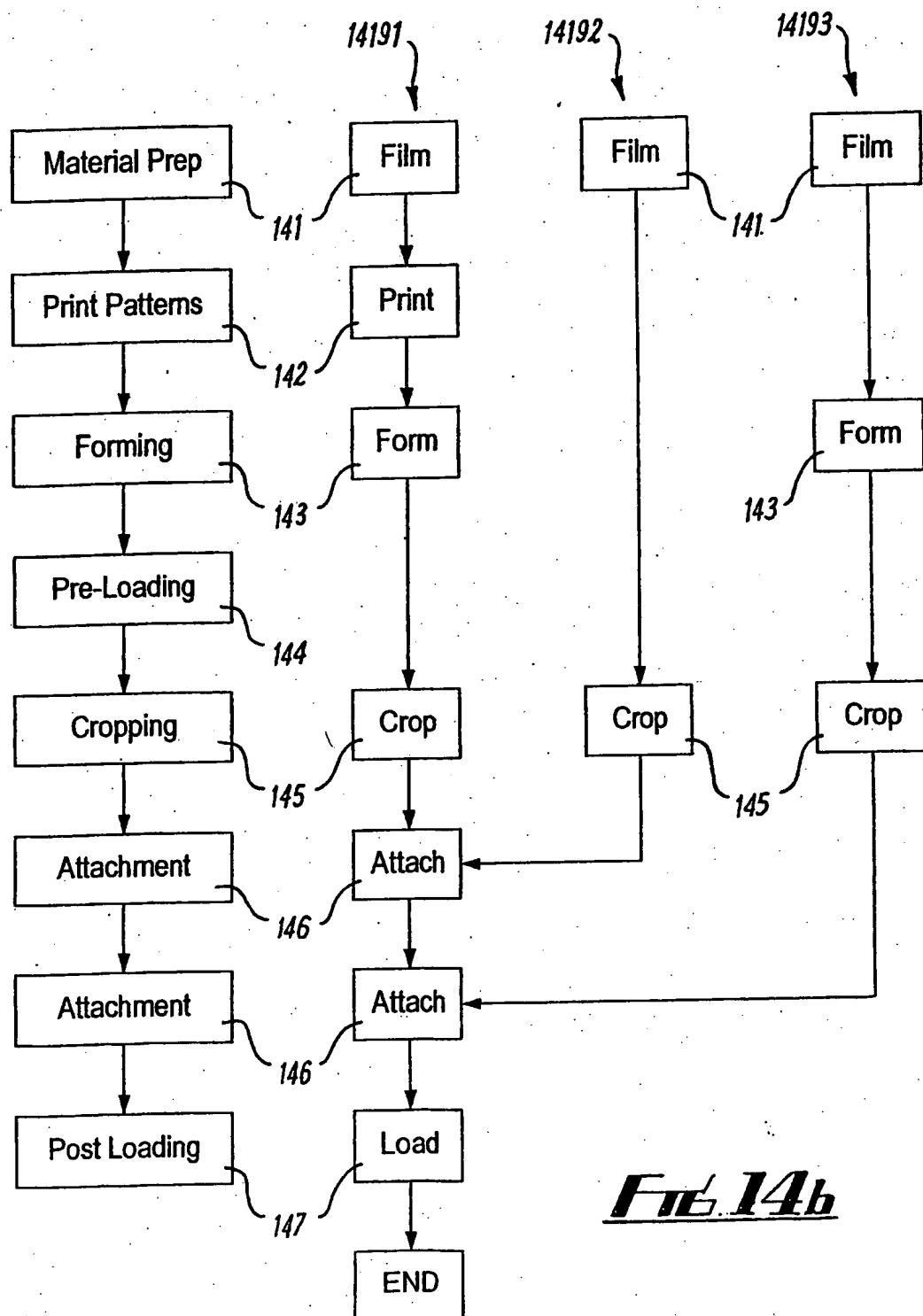
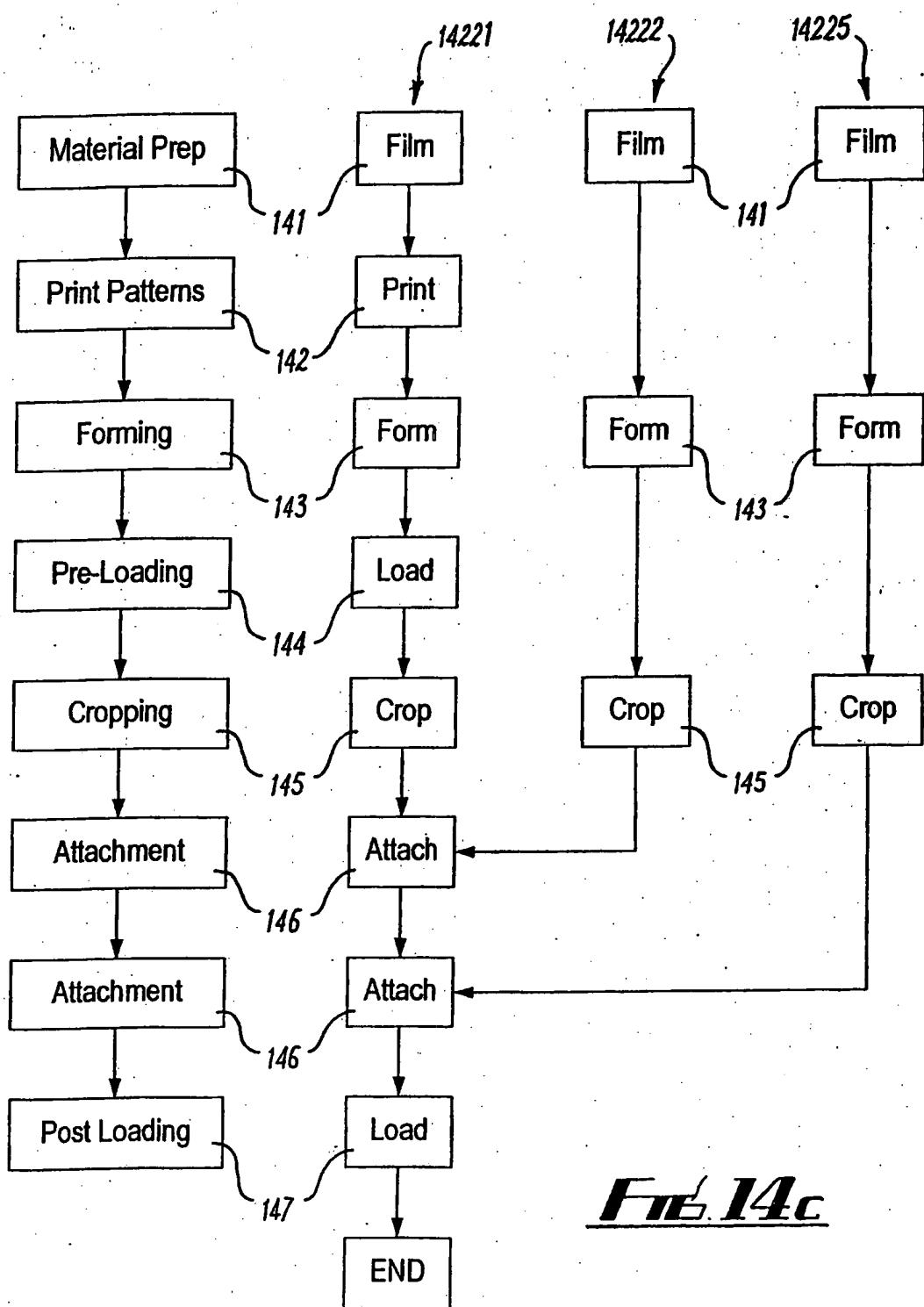
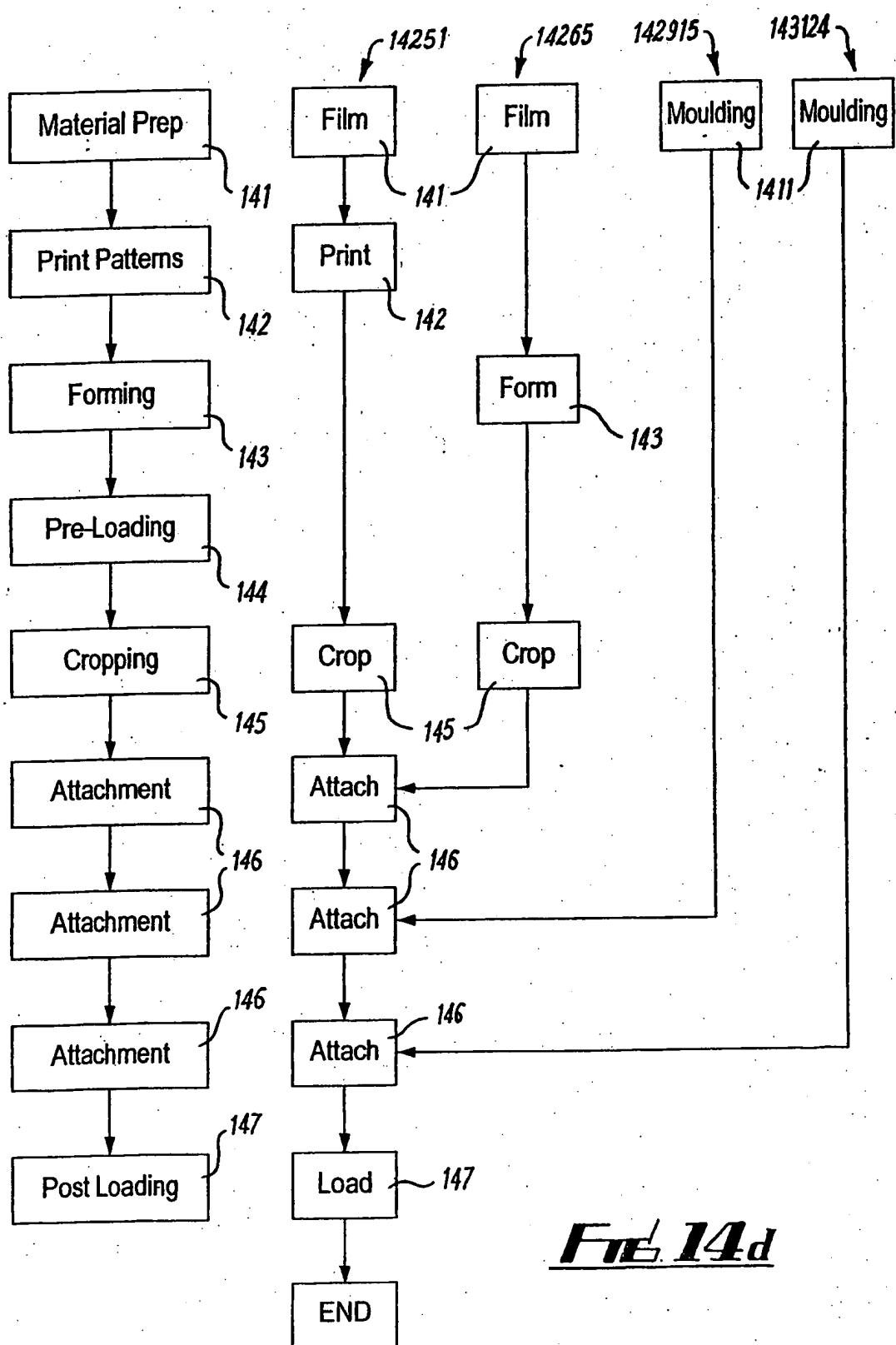


FIG 14a

*FIG 14b*

**FIG 14c**

**FIG. 14d**

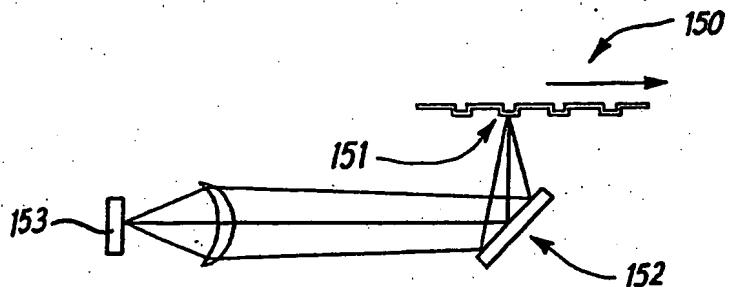


Fig. 15

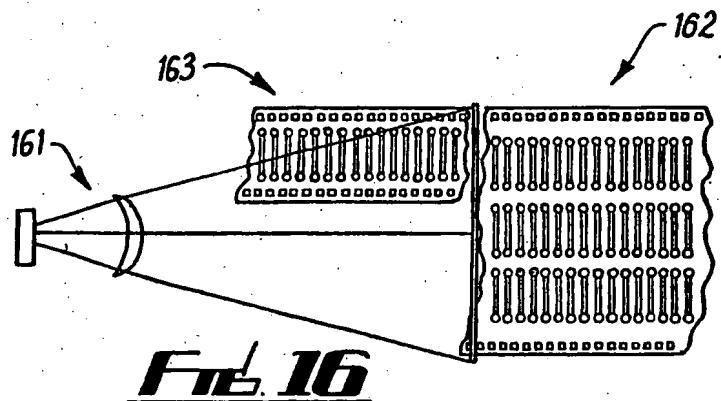
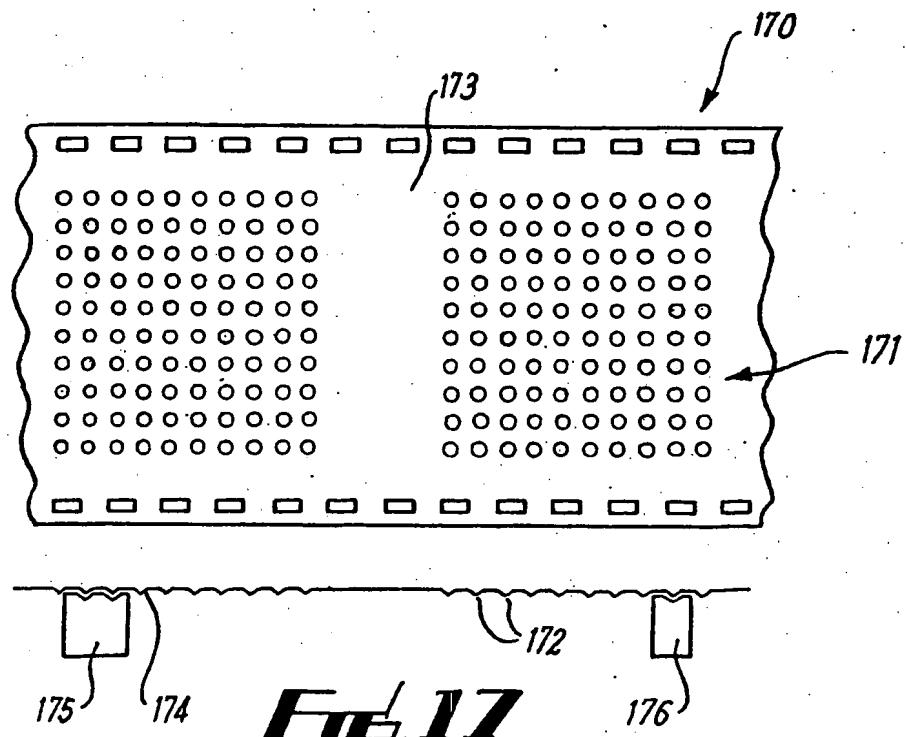


Fig. 16



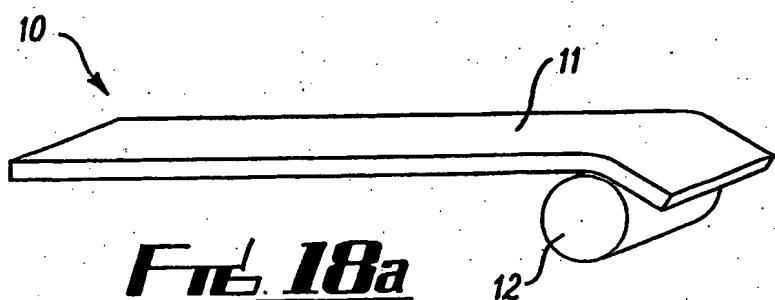


Fig. 18a

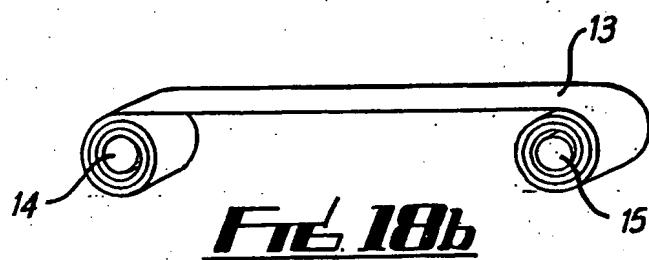


Fig. 18b



Fig. 18c

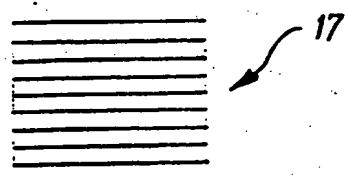


Fig. 18d

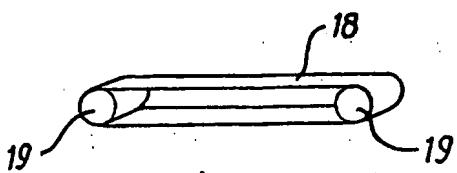


Fig. 18e

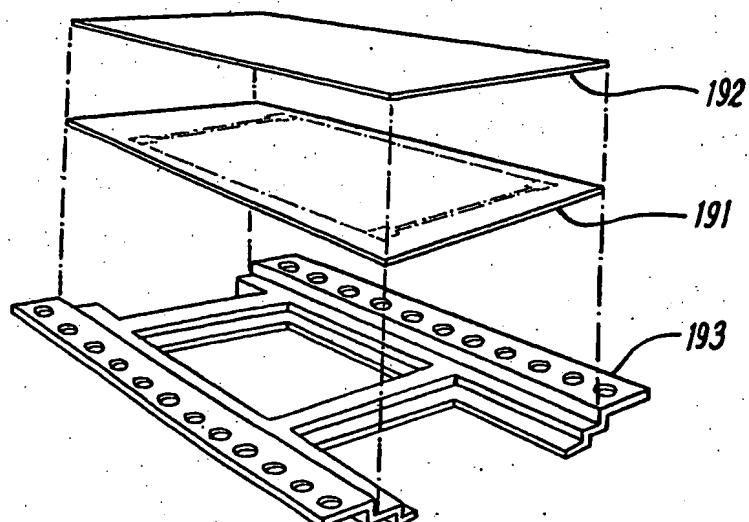


Fig. 19

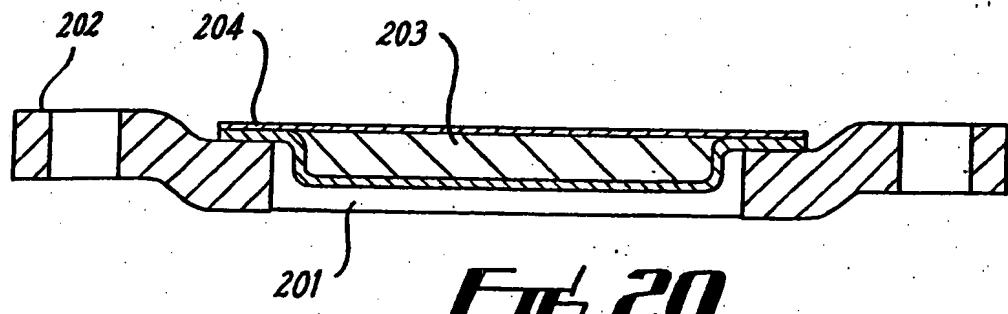


Fig. 20

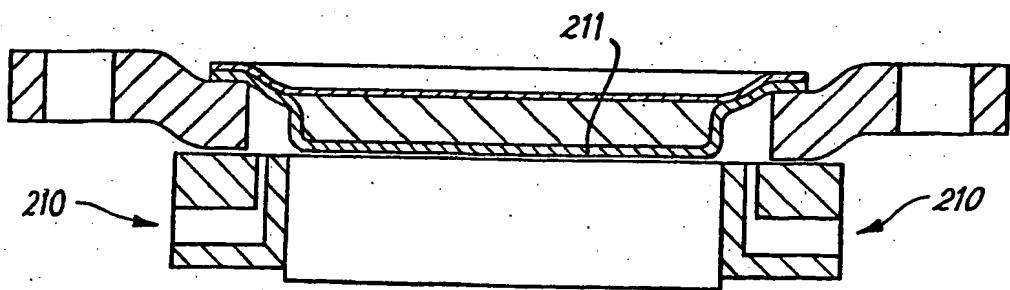
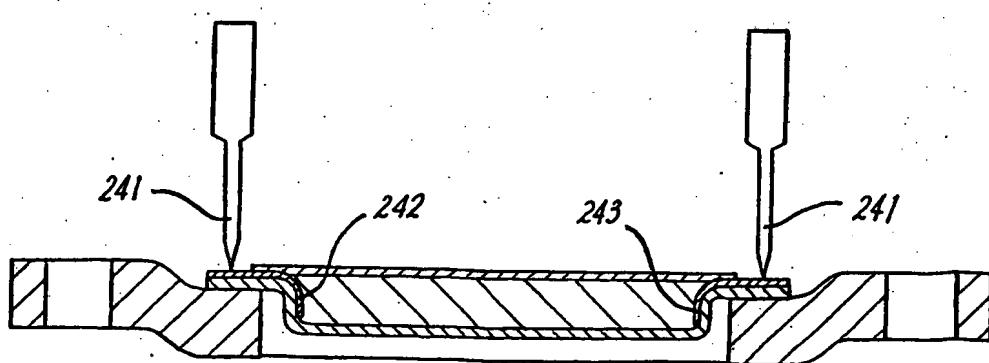
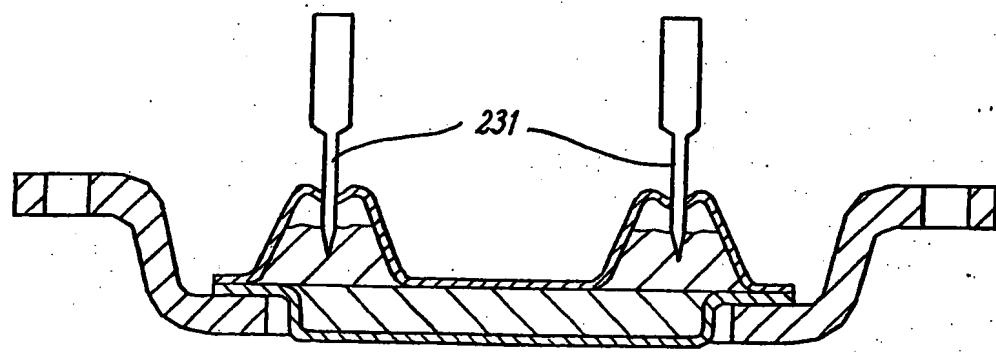
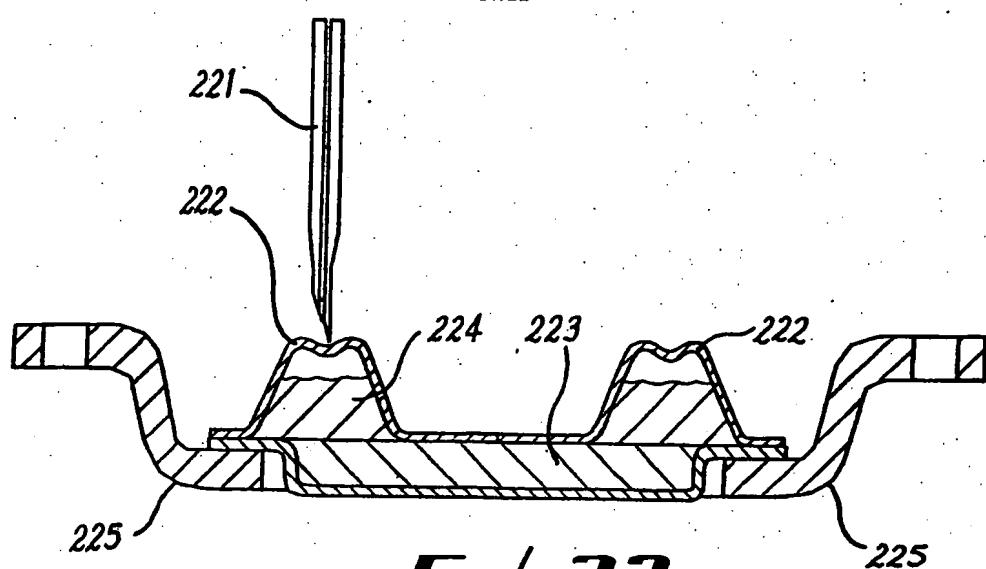
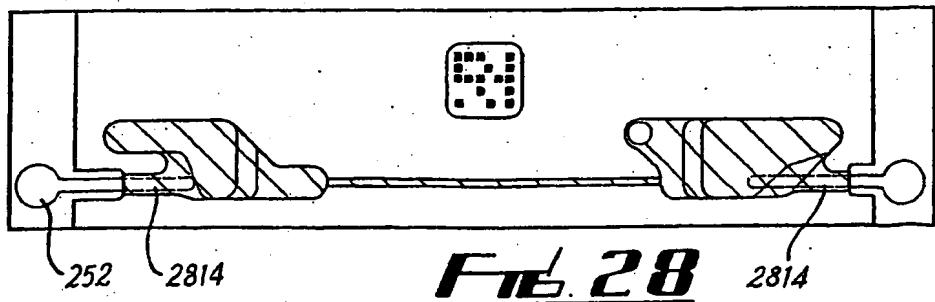
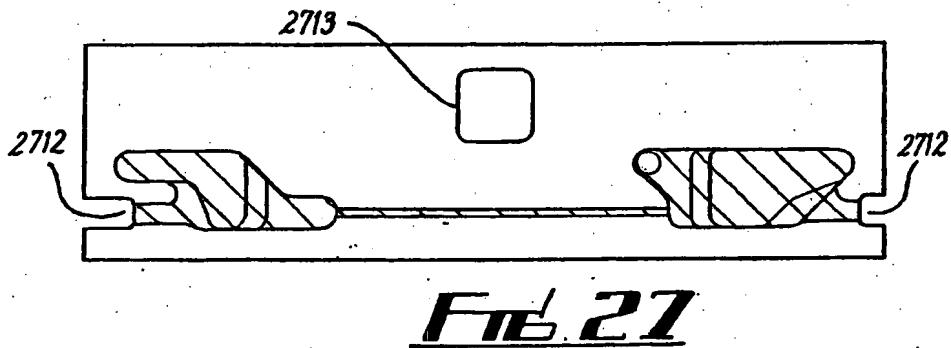
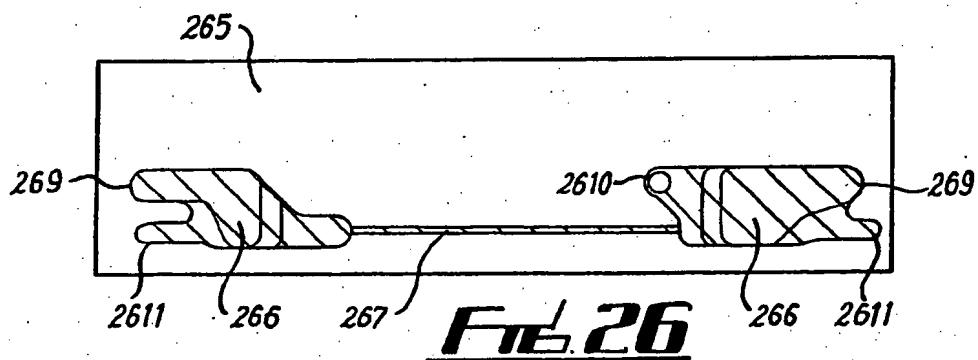
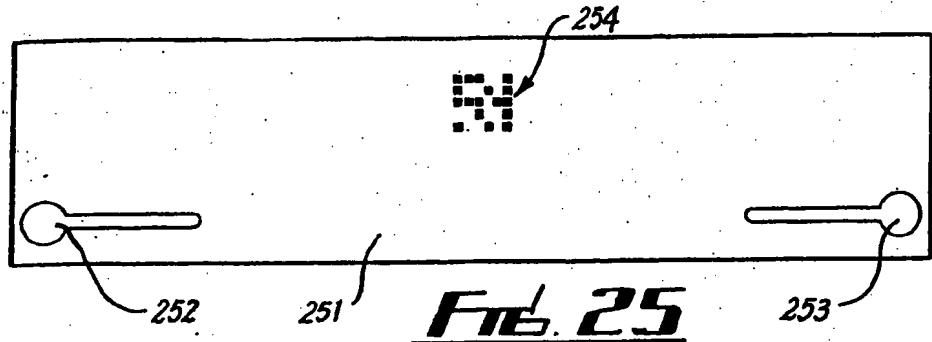
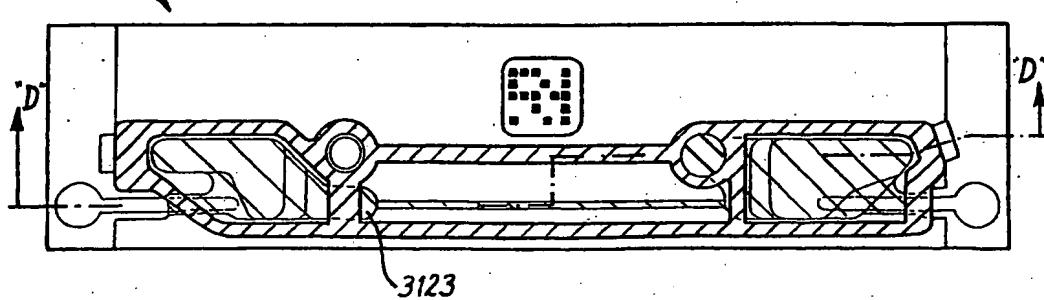
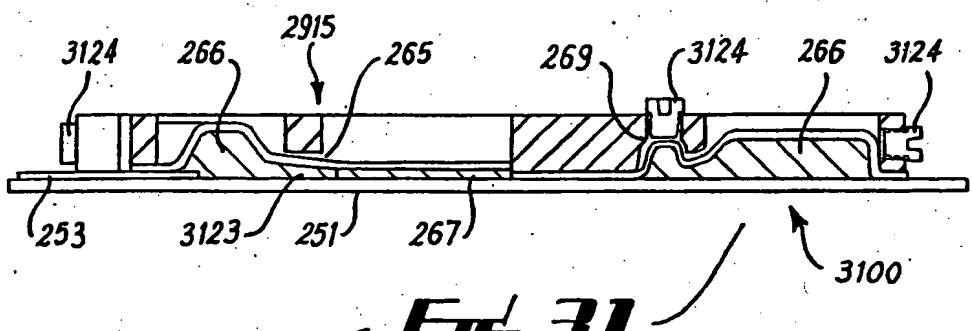
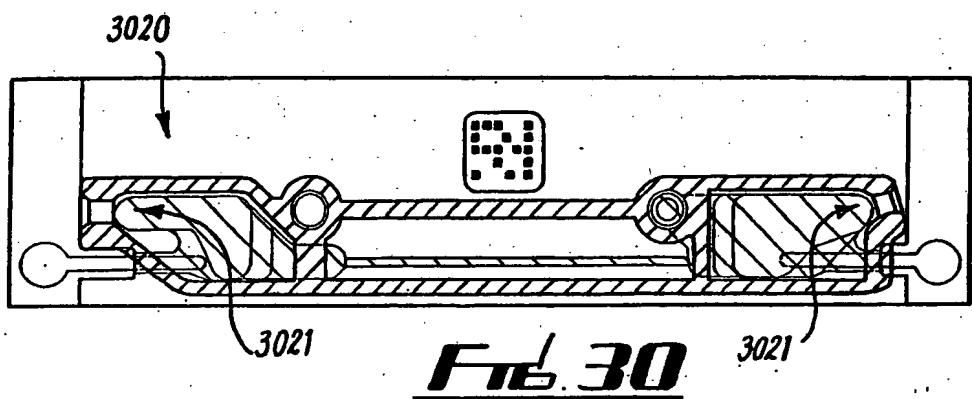
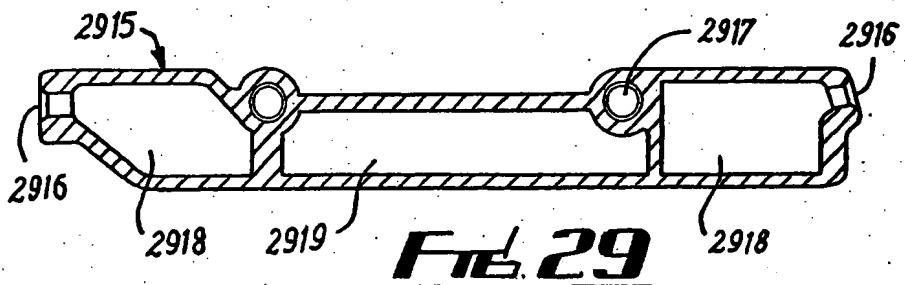


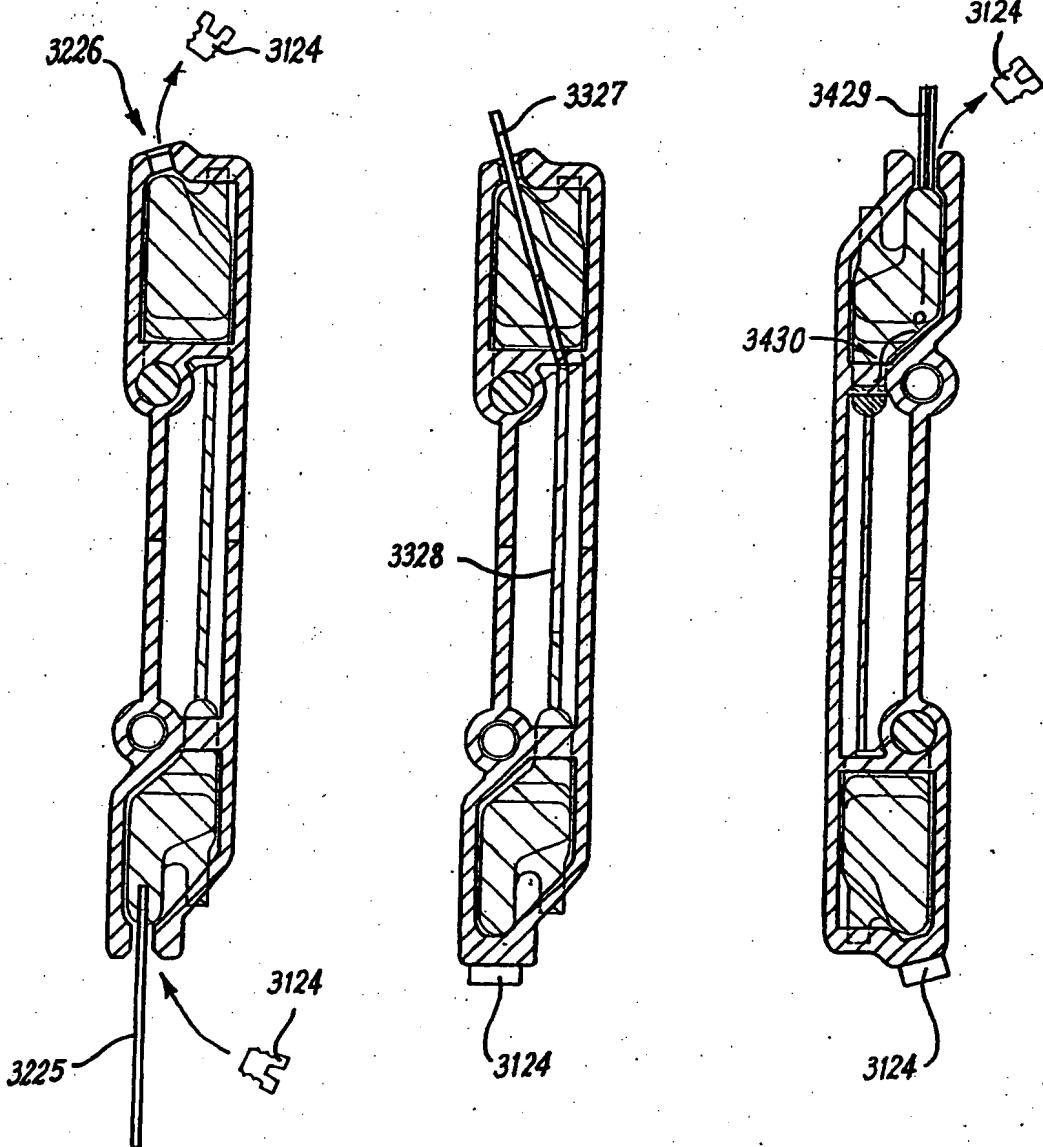
Fig. 21







SUBSTITUTE SHEET (RULE 26)

Fig. 32Fig. 33Fig. 34

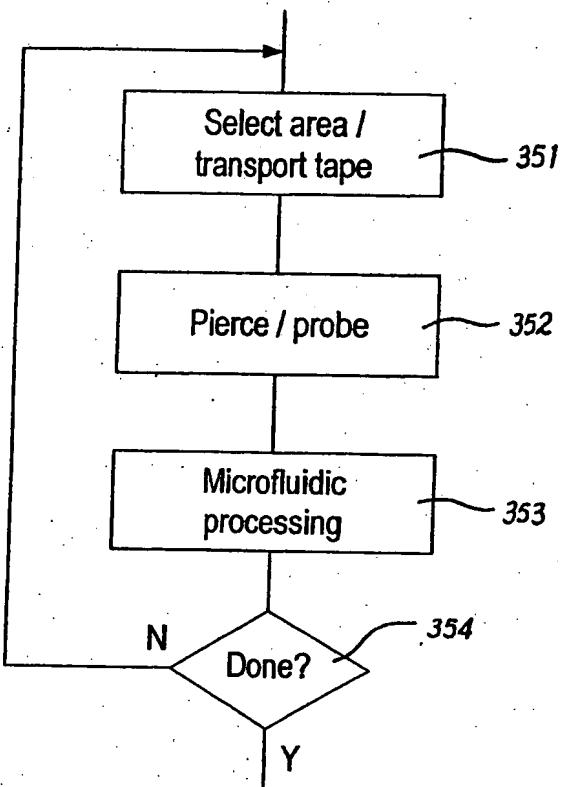


Fig. 35